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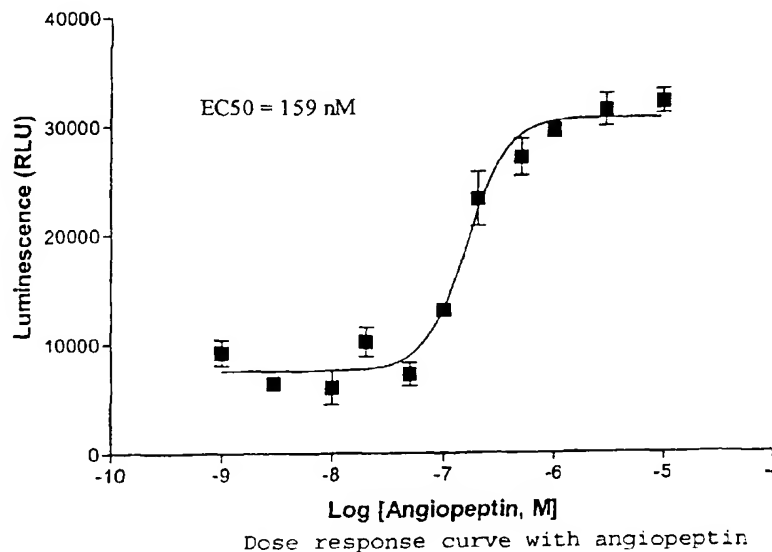
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[Continued on next page]

(54) Title: A RECOMBINANT CELL LINE EXPRESSING GPCR_{x11} AS A FUNCTIONAL RECEPTOR VALIDATED BY ANGIOPEPTIN AND USEFUL FOR SCREENING OF AGONISTS AND ANTAGONISTS



reference means. GPCR_{x11} cells gave a specific signal with synthetic angiopeptin and a somatostatin analog allowing to validate this cell line for screening of natural or synthetic agonists and antagonists. In parallel, extended tissue distribution and polyclonal antibodies have been produced to facilitate GPCR_{x11} characterisation.

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A RECOMBINANT CELL LINE EXPRESSING GPCR α 11 AS A FUNCTIONAL
RECEPTOR VALIDATED BY ANGIOPEPTIN AND USEFUL FOR SCREENING
OF AGONISTS AND ANTAGONISTS

10

Field of the invention

[0001] The present invention is related to a newly identified member of the superfamily of G-protein-coupled receptors as well as to the various uses that can be made
15 of said receptor.

[0002] The invention is also related to the polynucleic acid sequence (polynucleotide) encoding said receptor.

[0003] The invention is further related to methods
20 using receptor polypeptide and polynucleotide applicable to diagnostic and treatment in receptor-mediated disorders.

[0004] The invention is further related to drug-screening methods using the receptor polypeptide and polynucleotide, to identify agonists and antagonists
25 applicable to diagnostic, prevention and/or treatment of said various disorders.

[0005] The invention further encompasses unknown agonists and antagonists detected and recovered based on the receptor polypeptide and polynucleotide.

30 [0006] The invention is further related to procedures for producing the receptor polypeptide and

Background of the invention

[0007] G-protein coupled receptors (GPCRs) are proteins responsible for transducing a signal within a cell. GPCRs have usually seven transmembrane domains. Upon
5 binding of a ligand to an extra-cellular portion or fragment of a GPCR, a signal is transduced within the cell that results in a change in a biological or physiological property or behaviour of the cell. GPCRs, along with G-proteins and effectors (intracellular enzymes and channels
10 modulated by G-proteins), are the components of a modular signalling system that connects the state of intra-cellular second messengers to extra-cellular inputs.

[0008] GPCR genes and gene products are potential causative agents of disease and these receptors seem to be
15 of critical importance to both the central nervous system and peripheral physiological processes.

[0009] The GPCR protein superfamily is represented in five families : Family I, receptors typified by rhodopsin and the beta2-adrenergic receptor and currently
20 represented by over 200 unique members; Family II, the parathyroid hormone/calcitonin/secretin receptor family; Family III, the metabotropic glutamate receptor family, Family IV, the CAMP receptor family, important in the chemotaxis and development of *D. discoideum*; and Family V,
25 the fungal mating pheromone receptor such as STE2.

[0010] G proteins represent a family of heterotrimeric proteins composed of α , β and γ subunits, that bind guanine nucleotides. These proteins are usually linked to cell surface receptors (receptors containing
30 seven transmembrane domains).

[0011] Following ligand binding to the GPCR a

which caused the α -subunit to exchange a bound GDP molecule for a GTP molecule and to dissociate from the $\beta\gamma$ -subunits.

[0012] The GTP-bound form of the α , β and γ -subunits typically functions as an effector-modulating moiety, leading to the production of second messengers, such as cAMP (e.g. by activation of adenyl cyclase), diacylglycerol or inositol phosphates.

[0013] Greater than 20 different types of α -subunits are known in humans. These subunits associate with a small pool of β and γ subunits. Examples of mammalian G proteins include Gi, Go, Gq, Gs and Gt. G proteins are described extensively in Lodish et al., *Molecular Cell Biology*, (Scientific American Books Inc., New York, N.Y., 1995), the contents of which are incorporated herein by reference.

[0014] Known and unknown GPCRs constitute now major targets for drug action and development.

[0015] Therefore, it exists a need for providing new G protein coupled receptors which could be used for the screening of new agonists and antagonists having advantageous potential prophylactic and therapeutical properties.

[0016] More than 300 GPCRs have been cloned thus far and it is generally assumed that it exists well over 1000 such receptors. Mechanistically, approximately 50-60% of all clinically relevant drugs act by modulating the functions of various GPCRs (Cudermann et al., *J. Mol. Med.*, Vol. 73, pages 51-63, 1995).

Summary of the invention

[0017] The present invention is related to newly identified member of G-protein-coupled receptor, preferably a human receptor, as well as to the polynucleotide sequence
5 encoding said human receptor described hereafter (SEQ ID NO. 1 and 2).

[0018] The present invention is also related to other newly identified members of G-protein-coupled receptors, preferably human receptors, as well as to the
10 polynucleotide sequence encoding said other human receptor described hereafter (SEQ ID NO. 3 to SEQ ID NO. 22).

[0019] The present invention is also related to nucleotidic and/or amino acid sequence homologous to the sequences corresponding to the receptor described
15 hereafter.

[0020] An homologous sequence (which may exist in other mammal species) means a sequence which presents a high sequence identity or homology (which presents an identity higher than 70%, 75%, 80%, 85%, 90% or 95%) with
20 the complete human sequence described hereafter, and preferably characterised by a similar pharmacology, especially a preference for binding angiopeptin and/or somatostatin analogs.

[0021] Another aspect of the present invention is
25 related to a specific active portion of said sequence. Said active portion could be a receptor which comprises a partial deletion upon the complete nucleotide or amino acid sequence and which still maintains the active site(s) necessary for the binding of specific ligands able to
30 interact with said receptor.

[0022] Homologous sequences of the sequence

specific human populations, but which are involved in the same biochemical pathway.

[0023] Such homologous sequences may comprise addition, deletion or substitution of one or more amino acids or nucleotides, which does not substantially alter the functional characteristics of the receptor according to the invention.

[0024] Thus, the invention encompasses also a receptor and corresponding nucleotide sequence having exactly the same amino acid or nucleotide sequences as shown in the enclosed sequence listing, as well as molecules which differ, but which are retaining the basic qualitative binding properties of the complete receptor according to the invention.

[0025] The invention is preferably related to said (human) receptor characterised by the complete nucleotide and amino acid sequences described hereafter, to unknown (and not previously described in the state of the art) agonist, reverse agonist and antagonist compounds or inhibitors of said receptor. Preferably, said inhibitors are antisens RNAs, rybozymes or antibodies (or specific hypervariable (FAB, FAB'2, ...) portions thereof) that bind specifically to said receptor or its encoding nucleotide sequence (i.e. that have at least a 10 fold greater affinity for said receptors than any other naturally occurring antibody). Said specific antibodies are preferably obtained by a process involving the injection of a pharmaceutically acceptable preparation of such amino acid sequence into a animal capable of producing antibodies directed against said receptor.

[0026] For instance, a monoclonal antibody directed

encoding said receptor into a mouse and than fusing mouse spleen cells with myeloma cells.

[0027] The present invention is also related to the polynucleotide according to the invention, possibly linked
5 to other expression sequences and incorporated into a vector (plasmids, viruses, liposomes, cationic vesicles,...) and host cells transformed by such vector.

[0028] The present invention is also related to the recombinant, preferably human receptor according to the
10 invention, produced by such host cells according to the method well known by the person skilled in the art, as well as a functional assay (diagnostic kit) comprising all the means and media for the identification of the receptor, its nucleotide sequence, as well as agonist, reverse agonist,
15 antagonist and inhibitor of said receptor or its nucleotide sequence. Said diagnostic kit comprises preferably the following elements : the receptor, its encoding nucleotide sequence, antibodies directed against said receptor or its nucleotide sequence, as well as possible agonist, reverse
20 agonist, antagonist or inhibitor compounds of said receptor. Said diagnostic kit comprises means and media for performing said diagnostic preferably through a measure of dosage/activity of said receptor, by genetic analysis of the receptor nucleotide sequence, preferably by RT/PCR or
25 by immuno-analysis, preferably by the use of antibodies directed against said receptor.

[0029] The present invention is also related to a transgenic non-human mammal comprising a partial or total deletion of the genetic sequence encoding the receptor
30 according to the invention, preferably a non human mammal comprising an homologous recombination "knock-out" of the

(event...) transgenic non-human mammal overexpressing above natural level said polynucleotide sequence.

[0030] Said transgenic non-human mammal can be obtained by methods well known by the person skilled in the art, for instance by the one described in the document W098/20112 using classical techniques based upon the
5 transfection of embryonic stem cells, preferably according to the method described by Carmeliet et al., Nature, Vol. 380, p. 435-439, 1996.

[0031] Preferably, in said transgenic non human mammal overexpressing, the polynucleotide according to the
10 invention or active portions thereof has been previously incorporated in a DNA construct with an inducible promoter allowing its overexpression and possibly with tissues and other specific regulatory elements.

[0032] Another aspect of the present invention is
15 related to a method and kit for performing said method for the screening (detection and possibly recovering) of compounds or a natural extract which are unknown (not yet described in the state of the art) or not known to be agonists, reverse agonists, antagonists or inhibitors of
20 natural compounds to the receptor according to the invention, said method comprising :

- contacting a cell or cell extract from the cell transfected with a vector expressing the polynucleotide encoding the receptor according to the invention or
25 active portion(s) thereof,
- possibly isolating a membrane fraction from the cell extract or the complete cell with a compound or molecules present in said natural extract under conditions permitting binding of said compound or said
30 mixture of molecules to said receptor, possibly by the

said compound or said mixture of molecules to said receptor by means of a bioassay, (preferably a

modification in the production of a second messenger or an increase in the receptor activity) in the presence of another compound working as an agonist, reverse agonist, antagonist or inhibitor to the receptor according to the invention and thereby possibly recovering and determining whether said compound or mixture of molecules is (are) able to work as agonist, reverse agonist, antagonist, or inhibitor of the compound to its receptor.

10 [0033] Preferably, the second messenger assay comprises the measurement of intra-cellular cAMP, intracellular inositol phosphates, intra-cellular diacylglycerol concentrations, arachinoid acid concentration, MAP kinase(s) or tyrosine kinase(s) pathways
15 activation or intra-cellular calcium mobilisation.

[0034] Preferably, said bioassay is validated by the addition of angiopeptin and any other suitable related peptides to the receptor according to the invention by a method well-known by the person skilled in the art and
20 described hereafter.

[0035] The screening method according to the invention could be performed by well known methods to the person skilled in the art, preferably by high-throughput screening, diagnostic and dosage devices based upon the
25 method described in the International patent application WO00/02045 performed upon various solid supports such as micro-titer plates or biochips (microarrays) according to known techniques by the person skilled in the art.

[0036] The present invention is also related to the
30 known or unknown compound or molecules characterised and possibly recovered by said method for its (their) use as a

or molecule(s) and a pharmaceutically acceptable carrier or

diluent for the preparation of a medicament in the prevention and/or the treatment of various diseases.

[0037] In the pharmaceutical composition, the carrier or the adequate pharmaceutical carrier or diluant
5 can be any solid, liquid or gaseous support which is non-toxic and adapted for the administration (in vivo or ex vivo) to the patient, including the human, through various administration roots such as oral administration, intravenous administration, intradermal administration,
10 etc.

[0038] Said pharmaceutical composition may comprise also various vesicles or adjuvants well known by the person skilled in the art, able to modulate the immune response of the patient. The percentage of active compound-molecules/ pharmaceutical carriers can vary, the range being only limited by the tolerance and the efficiency of the active compounds to the patient. Said ranges of administration are also limited by the frequency of administration and the possible side effects of the compound or molecules.

20 [0039] A further aspect of the present invention is related to said unknown compound or molecule(s) identified by said screening method, to the pharmaceutical composition comprising it and to their use in the treatment of viral infections or diseases induced by various viruses or
25 bacteria, the treatment or prevention of disturbances of cell migration, diseases or perturbations of the immune system, including cancer, development of tumours and tumour metastasis, inflammatory and neo-plastic processes, bacterial and fungal infections, for wound and bone healing
30 and dysfunction of regulatory growth functions, pains, diabetes, obesity, anorexia, bulimia, acute heart failure.

atherosclerosis, diseases characterised by excessive smooth

muscle cell proliferation, aneurysms, wound healing, diseases characterised by loss of smooth muscle cells or reduced smooth muscle cell proliferation, stroke, ischemia, ulcers, allergies, benign prostatic hypertrophy, migraine, 5 vomiting, psychotic and neurological disorders, including anxiety, schizophrenia, maniac depression, depression, delirium, dementia and severe mental retardation, degenerative diseases, neurodegenerative diseases such as Alzheimer's disease or Parkinson's disease, and 10 dyskinesias, such as Huntington's disease or Gilles de la Tourette's syndrome and other related diseases.

[0040] Among the mentioned diseases the preferred applications are related to therapeutic agents targeting 7TM receptor that can play a function in preventing, 15 improving or correcting dysfunctions or diseases, including, but not limited to fertility, fetal development, infections such as bacterial, fungal, protozoan and viral infections, particularly infections caused by HIV1 and HIV2, pain, cancer, anorexia, bulimia, asthma, Parkinson's 20 disease, acute heart failure, hypertension, urinary retention, osteoporosis, angina pectoris, myocardial infarction, ulcers, asthma, allergies, benign prostatic hypertrophy, psychotic and neurological disorders including anxiety, depression, migraine, vomiting, stroke, 25 schizophrenia, manic depression, delirium, dementia, severe mental retardation and dyskinesias, such as Huntington's disease or Gilles de la Tourette's syndrome.

[0041] This invention relates to the use of a human G protein-coupled receptor as a screening tool to identify 30 agonists or antagonists of the aequorin luminescence resulting from expression of this receptor.

Example 1: Cloning of human GPCR_{x11} receptor

[0042] In order to identify and clone novel human GPCR (G-protein coupled receptor) the following approach was used. Sequences of the following GPCR: GPR8, ChemR23, HM74
 5 and GPR14 were used as queries to search for homologies in public high-throughput genomic sequence databases (NCBI).

[0043] Using the above strategies, a novel human sequence of GPCR was identified. We called this new GPCR: GPCR_{x11} (SEQ ID number 1 and 2).

10 [0044] In order to clone the GPCR_{x11} sequence we performed a polymerase chain reaction (PCR) on total human genomic DNA. Primers were synthesized based upon the GPCR_{x11} human sequence and were as follows:

15 SEQ ID 23 GPCR_{x11} fw: 5'-ccggaattcaccatggatccaaccaccccg-3'
 SEQ ID 24 GPCR_{x11} rv: 5'-ctagtctagactctacaccagactgcttctc-3'

[0045] Amplification resulted in a fragments of 0.99 kilobase containing the entire coding sequence of the
 20 GPCR_{x11} gene. This fragment was subcloned into the pCDNA3 (Invitrogen) vector for DNA sequencing analysis.

[0046] Nucleotide and deduced amino acid sequence of human GPCR_{x11} (SEQ ID NO 1)

25	1	M	D	P	T	T	P	A	W	G	T	E	S	T	T	V
15	1	ATG	GAT	CCA	ACC	ACC	CCG	GCC	TGG	GGA	ACA	GAA	AGT	ACA	ACA	GTG
45																
30	16	N	G	N	D	Q	A	L	L	L	L	C	G	K	E	T
30	46	AAT	GGA	AAT	GAC	CAA	GCC	CTT	CTT	CTG	CTT	TGT	GGC	AAG	GAG	ACC
90																
35	31	L	I	P	V	F	L	I	L	F	I	A	L	V	G	L
45																

136 GTA GGA AAC GGG TTT GTG CTC TGG CTC CTG GGC TTC CGC ATG CGC
180
61 R N A F S V Y V L S L A G A D
5 75
181 AGG AAC GCC TTC TCT GTC TAC GTC CTC AGC CTG GCC GGG GCC GAC
225
76 F L F L C F Q I I N C L V Y L
10 90
226 TTC CTC TTC CTC TGC TTC CAG ATT ATA AAT TGC CTG GTG TAC CTC
270
91 S N F F C S I S I N F P S F F
15 105
271 AGT AAC TTC TTC TGT TCC ATC TCC ATC AAT TTC CCT AGC TTC TTC
315
106 T T V M T C A Y L A G L S M L
20 120
316 ACC ACT GTG ATG ACC TGT GCC TAC CTT GCA GGC CTG AGC ATG CTG
360
121 S T V S T E R C L S V L W P I
25 135
361 AGC ACC GTC AGC ACC GAG CGC TGC CTG TCC GTC CTG TGG CCC ATC
405
136 W Y R C R R P R H L S A V V C
30 150
406 TGG TAT CGC TGC CGC CGC CCC AGA CAC CTG TCA GCG GTC GTG TGT
450
151 V L L W A L S L L L S I L E G
35 165
451 GTC CTG CTC TGG GCC CTG TCC CTA CTG CTG AGC ATC TTG GAA GGG
495
166 K F C G F L F S D G D S G W C
40 180
496 AAG TTC TGT GGC TTC TTA TTT AGT GAT GGT GAC TCT GGT TGG TGT
540
181 Q T F D F I T A A W L I F L F
45 195
541 CAG ACA TTT GAT TTC ATC ACT GCA GCG TGG CTG ATT TTT TTA TTC
585
196 M V L C G S S L A L L V R I L
50 210
586 ATG GTT CTC TGT GGG TCC AGT CTG GCC CTG CTG GTC AGG ATC CTC
630
211 C G S R G L P L T R L Y L T I
55 225
240

720 676 CTG CTC ACA GTG CTG GTG TTC CTC CTC TGC GGC CTG CCC TTT GGC
 5 255 241 I Q W F L I L W I W K D S D V
 765 721 ATT CAG TGG TTC CTA ATA TTA TGG ATC TGG AAG GAT TCT GAT GTC
 10 270 256 L F C H I H P V S V V L S S L
 810 766 TTA TTT TGT CAT ATT CAT CCA GTT TCA GTT GTC CTG TCA TCT CTT
 15 285 271 N S S A N P I I Y F F V G S F
 855 811 AAC AGC AGT GCC AAC CCC ATC ATT TAC TTC TTC GTG GGC TCT TTT
 20 300 286 R K Q W R L Q Q P I L K L A L
 900 856 AGG AAG CAG TGG CGG CTG CAG CAG CCG ATC CTC AAG CTG GCT CTC
 25 315 301 Q R A L Q D I A E V D H S E G
 945 901 CAG AGG GCT CTG CAG GAC ATT GCT GAG GTG GAT CAC AGT GAA GGA
 30 330 316 C F R Q G T P E M S R S S L V
 990 946 TGC TTC CGT CAG GGC ACC CCG GAG ATG TCG AGA AGC AGT CTG GTG
 35 331 331 *
 993 991 TAG

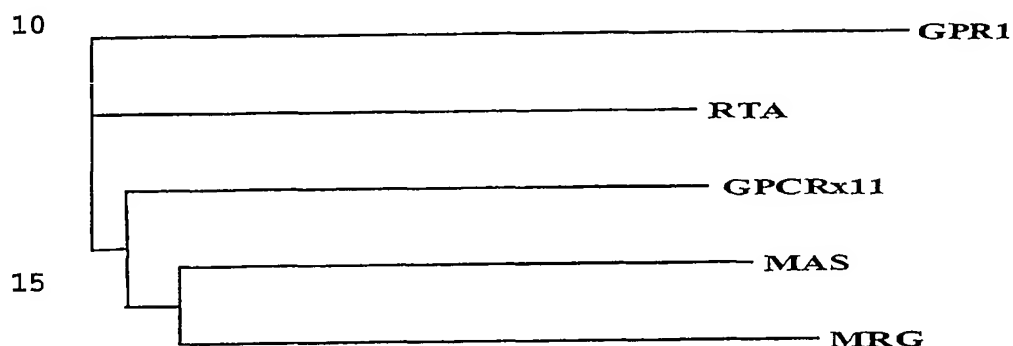
40 [0047] Amino acid sequence of human GPCR α 11 (330 amino acids) (SEQ ID NO:2). The seven predicted transmembrane domains are underlined.

45 MDPTTPAWGTESTTVNGNDQALLLLCGKETLIPVFLILFIALVGLVGNFVLWLLGFRM
 RRNAFSVYVLSLAGADFLFLCFQIINCLVYLSNFFCSISINFPSFFTTVMTCAYLAGLS
 MLSTVSTERCLSVLWPIWYRCRRPRHLSAVVCVLLWALSLLLSILEGKFCGFLFSDGDS
 GWCQTFDFITAAWLIFLFMVLCGSSLALLVRILCGSRGLPLTRLTYLTILLTVLVFLLCG
 LPFGIQWFLILWIWKDSDFLCHIHVSVVLSLSSANPIIYFFVGSFRKQWRLQQPI

[0048] At the amino acid sequence level, the human GPCR α 11 is 37% identical to the rat RTA receptor. The gene coding GPCR α 11 is located on chromosome 11.

Alignment of GPCR α 11 (fig.1)

- 5 [0049] Alignment of the amino acid sequence of GPCR α 11 with RTA and other RTA related sequences were performed using ClustalX algorithm. Then, the dendrogram was constructed using TreeView algorithm.



Tissular distribution of GPCR α 11

- 20 [0050] Reverse transcription-polymerase chain reaction (RT-PCR) experiments were carried out using a panel of polyA⁺ RNA (Clontech). The primers were as follows: GPCR α 11 sense primer (SEQ ID NO 25: 5'-TTCTCTGTCTACGTCCTCAG-3') and GPCR α 11 antisense primer (SEQ
25 ID NO 26: 5'-GTCCTGTCATCTCTTAACAG-3'). The expected size of the amplified DNA band was 586 bp. Approximately 75 ng of poly A⁺ RNA was reverse transcribed with superscript II (Life Technologies) and used for PCR. PCR was performed under the following conditions: denaturation at 94°C for 3
30 min, 38 cycles at 94°C for 1 min, 58°C for 2 min and 72°C

[0051] GPCR α 11 mRNA was assayed by RT-PCR in 16 human tissues. A strong band of expected size (586 bp) was detected in testis, at lower levels in uterus and thymus, while not in pituitary gland, spinal cord, pancreas, small intestine, placenta, stomach, liver, lung, spleen, brain, heart, kidney and skeletal muscle.

Functional assay for GPCR α 11

[0052] GPCR α 11 expressing clones have been obtained by transfection of CHO-K1 cells coexpressing mitochondrial apoaeguorin and Galpha $_{16}$, limit dilution and selection by northern blotting. Positive clones were used for screening with a reference peptidic library containing 250 peptides and neuropeptides at a concentration of 100 nM. A specific activity was obtained with angiopeptin (D-NaI-Cys-Tyr-D-trp-Lys-Val-Cys-Thr-NH $_2$ with a disulfide bridge between the two cysteines) and confirmed by a dose response curve (see figure 1). Additional related peptides were tested using the same cells. Amongst the different peptides tested, somatostatin analog (D2-NaI-Cys-Tyr-D-trp-Lys-Val-Cys-D2-NaI-NH $_2$) exhibited similar affinity. Somatostatin 14 has no activity on GPCR α 11.

Material. All chemicals were obtained from Sigma, unless stated. The cell culture media were from Gibco BRL and the peptides from Bachem

25 **Aequorin assays.** CHO-K1 cell lines expressing GPCR α 11 receptors, Galpha $_{16}$ and mitochondrial apoaeguorin were established. A functional assay based on the luminescence of mitochondrial aequorin following intracellular Ca $^{2+}$ release (1) was performed. Cells were seeded in 96 well plates and grown to confluence. Cells were then washed with PBS and resuspended in DMEM-F12 medium, incubated with 5 μ M Coelenterazine H (Molecular

Probes) for 4 hours at room temperature. Cells were then washed in DMEM-F12 medium and resuspended at a concentration of 0.5×10^6 cells/ml. Cells were then mixed with the peptides and the light emission recorded during 30 sec. using a Microlumat luminometer (Perkin Elmer). Results are expressed as Relative Light Units (RLU).

Antibodies

[0053] Antibodies directed against GPCR α 11 have been produced by repeated injections of plasmid encoding GPCR α 11 to mice. Serum has been collected following 5 injections and used for flow cytometry analysis with cells transfected with GPCR α 11. Several sera were positive and can be used for immunohistochemistry and other related applications

15 Example 2 : Cloning of the other sequences related to G-protein-coupled receptors

[0054] In order to identify and clone novel human DNA sequences related to GPCR, the following approach was used. Sequences of the following GPCR: GPR8, ChemR23, HM74 and GPR14 were used as queries to search for homologies in public high-throughput genomic sequence databases (NCBI).

[0055] Using the above strategies, ten novel human sequences of GPCR were identified. None of these clones contain introns :

25

GPCR α 2, SEQ ID NO 3

GPCR α 5, SEQ ID NO 5

GPCR α 7, SEQ ID NO 7

GPCR α 9, SEQ ID NO 9

30 GPCR α 14, SEQ ID NO 11

GPCR α 16, SEQ ID NO 13

GPCR α 18, SEQ ID NO 17

GPCRx19, SEQ ID NO 19

GPCRx20, SEQ ID NO 21

[0056] In order to clone these GPCR_x sequences, a
5 polymerase chain reaction (PCR) was performed on total
human genomic DNA. Primers were synthesized based upon the
human sequences described above and were as follows:

SEQ ID NO 27 GPCR_x2 fw: 5'-ccggaattcaccatggagtcctcacccatc-3'

10 SEQ ID NO 28 GPCR_x2 rv: 5'-ctagtctagacatcatgactccagccggg-3'

SEQ ID NO 29 GPCR_x5 fw: 5'-ccggaattcaccatggatccaaccatctcaacc-3'

SEQ ID NO 30 GPCR_x5 rv: 5'-ctagtctagatcactgctccaatctgcttc-3'

15 SEQ ID NO 31 GPCR_x7 fw:

5'-ccggaattcaccatgaaccagactttgaatagcagtgg-3'

SEQ ID NO 32 GPCR_x7 rv:

5'-ctagtctagatctcaagccccatctcattgggtgccc-3'

20 SEQ ID NO 33 GPCR_x9 fw: 5'-ccggaattcaccatggaagctgacctgg-3'

SEQ ID NO 34 GPCR_x9 rv: 5'-ctagtctagactcacgtggggcctgcgcc-3'

SEQ ID NO 35 GPCR_x14 fw: 5'-ccggaattcgccatgtacaacgggtcg-3'

SEQ ID NO 36 GPCR_x14 rv: 5'-ctagtctagattcagtgccactcaacaatg-3'

25 [0057] Amplification resulted in a fragments of
approximately 1 - 1.5 kilobase containing the entire coding
sequence of the human genes. These fragments obtained were
subcloned into the pCDNA3 (Invitrogen) vector for DNA
sequencing analysis.

30

Tissue distribution of identified (GPCR_x) receptors

[0058] To determine the tissue distribution of different

35 isolated from human tissues (Clontech). The oligo(dT)

primer was used in the reverse transcription step. Then, different GPCR α cDNA were amplified with specific primers.

	GPCR α 2	GPCR α 7	GPCR α 9	GPCR α 14	GPCR α 16	GPCR α 17	GPCR α 18	GPCR α 19	GPCR α 20
Li	-	-	-	-	-	-	-	-	+
Lu	+/-	-	+	+	-	++	-	-	++
Sp	-	-	++	+	-	-	-	-	+
Te	-	+	-	++	-	++	-	+/-	+
Br	++	-	-	-	-	-	++	-	++
He	-	-	-	-	-	-	-	-	++
Ki	+/-	-	-	+	-	++	-	-	+
Sk.m	-	-	-	-	-	+	-	-	++
Pi.G	-	-	-	-	-	-	++	+/-	+
Sp.C	++	-	-	-	-	++	+/-	+/-	+/-
Th	+/-	-	+	-	-	++	-	-	++
Pa	-	-	-	-	-	++	+/-	-	-
S.In	+/-	-	+	-	-	++	-	-	+
Ut	-	-	-	-	-	++	-	+/-	+
Pl	-	-	-	++	++	-	-	-	+
St	-	-	+	+/-	-	++	-	-	+

5

Table 1: Tissue distribution of GPCR α s: The presence or absence of different GPCR α was determined by RT-PCR analysis. ++, strong signal; +, signal clearly detected; +/-, weak signal; -, signal not detected. The tissues are the following: Li, liver; Lu, lung; Sp, Spleen; Te, testis; Br, Brain; He, Heart; Ki, Kidney; Sk.M, Skeletal muscle; Pi.G, Pituitary gland; Sp.C, spinal cord; Th, Thymus; Pa,

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5
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10

Nucleotide and deduced amino acid sequence of human GPCR α 2 (SEQ ID NO: 3 and 4 respectively)

1	M	E	S	S	P	I	P	Q	S	S	G	N	S	S	T	15
1	ATG	GAG	TCC	TCA	CCC	ATC	CCC	CAG	TCA	TCA	GGG	AAC	TCT	TCC	ACT	45
16	L	G	R	V	P	Q	T	P	G	P	S	T	A	S	G	30
46	TTG	GGG	AGG	GTC	CCT	CAA	ACC	CCA	GGT	CCC	TCT	ACT	GCC	AGT	GGG	90
31	V	P	E	V	G	L	R	D	V	A	S	E	S	V	A	45
91	GTC	CCG	GAG	GTG	GGG	CTA	CGG	GAT	GTT	GCT	TCG	GAA	TCT	GTG	GCC	135
46	L	F	F	M	L	L	L	D	L	T	A	V	A	G	N	60
136	CTC	TTC	TTC	ATG	CTC	CTG	CTG	GAC	TTG	ACT	GCT	GTG	GCT	GGC	AAT	180
61	A	A	V	M	A	V	I	A	K	T	P	A	L	R	K	75
181	GCC	GCT	GTG	ATG	GCC	GTG	ATC	GCC	AAG	ACG	CCT	GCC	CTC	CGA	AAA	225
76	F	V	F	V	F	H	L	C	L	V	D	L	L	A	A	90
226	TTT	GTC	TTC	GTC	TTC	CAC	CTC	TGC	CTG	GTG	GAC	CTG	CTG	GCT	GCC	270
91	L	T	L	M	P	L	A	M	L	S	S	S	A	L	F	105
271	CTG	ACC	CTC	ATG	CCC	CTG	GCC	ATG	CTC	TCC	AGC	TCT	GCC	CTC	TTT	315
106	D	H	A	L	F	G	E	V	A	C	R	L	Y	L	F	120
316	GAC	CAC	GCC	CTC	TTT	GGG	GAG	GTG	GCC	TGC	CGC	CTC	TAC	TTG	TTT	360
121	L	S	V	C	F	V	S	L	A	I	L	S	V	S	A	135
361	CTG	AGC	GTG	TGC	TTT	GTC	AGC	CTG	GCC	ATC	CTC	TCG	GTG	TCA	GCC	405
136	I	N	V	E	R	Y	Y	Y	V	V	H	P	M	R	Y	150
406	ATC	AAT	GTG	GAG	CGC	TAC	TAT	TAC	GTA	GTC	CAC	CCC	ATG	CGC	TAC	450
151	E	V	R	M	T	L	G	L	V	A	S	V	L	V	G	165
451	GAG	GTG	CGC	ATG	ACG	CTG	GGG	CTG	GTG	GCC	TCT	GTG	CTG	GTG	GGT	495
166	V	W	V	K	A	L	A	M	A	S	V	P	V	L	G	180
496	GTG	TGG	GTG	AAG	GCC	TTG	GCC	ATG	GCT	TCT	GTG	CCA	GTG	TTG	GGA	540
181	R	V	S	W	E	E	G	A	P	S	V	P	P	G	C	195
541	AGG	GTC	TCC	TGG	GAG	GAA	GGA	GCT	CCC	AGT	GTC	CCC	CCA	GGC	TGT	585
196	S	L	Q	W	S	H	S	A	Y	C	Q	L	F	V	V	210
586	TCA	CTC	CAG	TGG	AGC	CAC	AGT	GCC	TAC	TGC	CAG	CTT	TTT	GTG	GTG	630
211	V	F	A	V	L	Y	F	L	L	P	L	L	L	I	L	225
631	GTC	TTT	GCT	GTC	CTT	TAC	TTT	CTG	TTG	CCC	CTG	CTC	CTC	ATA	CTT	675
226	V	V	Y	C	S	M	F	R	V	A	R	V	A	A	M	240
676	GTG	GTC	TAC	TGC	AGC	ATG	TTC	CGA	GTG	GCC	CGC	GTG	GCT	GCC	ATG	720
241	Q	H	G	P	L	P	T	W	M	E	T	P	R	Q	R	255
721	CAG	CAC	GGG	CCG	CTG	CCC	ACG	TGG	ATG	GAG	ACA	CCC	CGG	CAA	CGC	765

271	A	P	Q	T	T	P	H	R	T	F	G	G	G	K	A	285
811	GCC	CCC	CAG	ACC	ACC	CCA	CAC	CGG	ACG	TTT	GGG	GGA	GGG	AAA	GCA	855
286	A	V	V	L	L	A	V	G	G	Q	F	L	L	C	W	300
856	GCA	GTG	GTT	CTC	CTG	GCT	GTG	GGG	GGA	CAG	TTC	CTG	CTC	TGT	TGG	900
301	L	P	Y	F	S	F	H	L	Y	V	A	L	S	A	Q	315
901	TTG	CCC	TAC	TTC	TCT	TTC	CAC	CTC	TAT	GTT	GCC	CTG	AGT	GCT	CAG	945
316	P	I	S	T	G	Q	V	E	S	V	V	T	W	I	G	330
946	CCC	ATT	TCA	ACT	GGG	CAG	GTG	GAG	AGT	GTG	GTC	ACC	TGG	ATT	GGC	990
331	Y	F	C	F	T	S	N	P	F	F	Y	G	C	L	N	345
991	TAC	TTT	TGC	TTC	ACT	TCC	AAC	CCT	TTC	TTC	TAT	GGA	TGT	CTC	AAC	1035
346	R	Q	I	R	G	E	L	S	K	Q	F	V	C	F	F	360
1036	CGG	CAG	ATC	CGG	GGG	GAG	CTC	AGC	AAG	CAG	TTT	GTC	TGC	TTC	TTC	1080
361	K	P	A	P	E	E	E	L	R	L	P	S	R	E	G	375
1081	AAG	CCA	GCT	CCA	GAG	GAG	GAG	CTG	AGG	CTG	CCT	AGC	CGG	GAG	GGC	1125
376	S	I	E	E	N	F	L	Q	F	L	Q	G	T	G	C	390
1126	TCC	ATT	GAG	GAG	AAC	TTC	CTG	CAG	TTC	CTT	CAG	GGG	ACT	GGC	TGT	1170
391	P	S	E	S	W	V	S	R	P	L	P	S	P	K	Q	405
1171	CCT	TCT	GAG	TCC	TGG	GTT	TCC	CGA	CCC	CTA	CCC	AGC	CCC	AAG	CAG	1215
406	E	P	P	A	V	D	F	R	I	P	G	Q	I	A	E	420
1216	GAG	CCA	CCT	GCT	GTT	GAC	TTT	CGA	ATC	CCA	GGC	CAG	ATA	GCT	GAG	1260
421	E	T	S	E	F	L	E	Q	Q	L	T	S	D	I	I	435
1261	GAG	ACC	TCT	GAG	TTC	CTG	GAG	CAG	CAA	CTC	ACC	AGC	GAC	ATC	ATC	1305
436	M	S	D	S	Y	L	R	P	A	A	S	P	R	L	E	450
1306	ATG	TCA	GAC	AGC	TAC	CTC	CGT	CCT	GCC	GCC	TCA	CCC	CGG	CTG	GAG	1350
451	S	*														452
1351	TCA	TGA														1356

Amino acid sequence of human GPCR α 2 (451 amino acids) (SEQ ID NO: 4). The seven predicted transmembrane domaines are underlined.

MESSPIPQSSGNSSTLGRVPQTPGPSTASGVPEVGLRDVASESVALFFMLLLDLTAVAGNAAVMAVIAKTPALRKFFVFV
HLCLVDLLAALTLMPLAMLSSSALFDHALFGEVACRLYLFLSVCFVSLAILSVSAINVERYYYVHPMRYEVRMTLGLVA
SVLVGVVWKALAMASVPVLGRVSWEEGAPSVPPGCSLQWSHSAYCQLFVVVFAVLVFLPLLLILVYCSMFRVARVAAM
QHGPLPTWMETPRQRSESLSSRSTMTSSGAPQTTPHRTFGGGKAAVLLAVGGQFLLCWLPYFSFHLVVALSAQPISTG
QVESVVTWIGYFCFTSNPFFYGCLNRQIRGELSKQFVCFKPAPEEELRLPSREGSIEENFLQFLQGTGCPSESWVSRL
PSPKQEPVAVDFRIPGQIAEETSEFLEQQLTSDIIMSDSYLRPAASPRLES

At the amino acid sequence level, the human GPCR α 2 is 23% identical to the human histamine H2 receptor.

Nucleotide and deduced amino acid sequence of human GPCR \times 5 (SEQ ID NO: 5 and 6 respectively)

1	M	D	P	T	I	S	T	L	D	T	E	L	T	P	I	15
1	ATG	GAT	CCA	ACC	ATC	TCA	ACC	TTG	GAC	ACA	GAA	CTG	ACA	CCA	ATC	45
16	N	G	T	E	E	T	L	C	Y	K	Q	T	L	S	L	30
46	AAC	GGA	ACT	GAG	GAG	ACT	CTT	TGC	TAC	AAG	CAG	ACC	TTG	AGC	CTC	90
31	T	V	L	T	C	I	V	S	L	V	G	L	T	G	N	45
91	ACG	GTG	CTG	ACG	TGC	ATC	GTT	TCC	CTT	GTC	GGG	CTG	ACA	GGA	AAC	135
46	A	V	V	L	W	L	L	G	C	R	M	R	R	N	A	60
136	GCA	GTT	GTG	CTC	TGG	CTC	CTG	GGC	TGC	CGC	ATG	CGC	AGG	AAC	GCC	180
61	F	S	I	Y	I	L	N	L	A	A	A	D	F	L	F	75
181	TTC	TCC	ATC	TAC	ATC	CTC	AAC	TTG	GCC	GCA	GCA	GAC	TTC	CTC	TTC	225
76	L	S	G	R	L	I	Y	S	L	L	S	F	I	S	I	90
226	CTC	AGC	GGC	CGC	CTT	ATA	TAT	TCC	CTG	TTA	AGC	TTC	ATC	AGT	ATC	270
91	P	H	T	I	S	K	I	L	Y	P	V	M	M	F	S	105
271	CCC	CAT	ACC	ATC	TCT	AAA	ATC	CTC	TAT	CCT	GTG	ATG	ATG	TTT	TCC	315
106	Y	F	A	G	L	S	F	L	S	A	V	S	T	E	R	120
316	TAC	TTT	GCA	GGC	CTG	AGC	TTT	CTG	AGT	GCC	GTG	AGC	ACC	GAG	CGC	360
121	C	L	S	V	L	W	P	I	W	Y	R	C	H	R	P	135
361	TGC	CTG	TCC	GTC	CTG	TGG	CCC	ATC	TGG	TAC	CGC	TGC	CAC	CGC	CCC	405
136	T	H	L	S	A	V	V	C	V	L	L	W	A	L	S	150
406	ACA	CAC	CTG	TCA	GCG	GTG	GTG	TGT	GTC	CTG	CTC	TGG	GCC	CTG	TCC	450
151	L	L	R	S	I	L	E	W	M	L	C	G	F	L	F	165
451	CTG	CTG	CGG	AGC	ATC	CTG	GAG	TGG	ATG	TTA	TGT	GGC	TTC	CTG	TTC	495
166	S	G	A	D	S	A	W	C	Q	T	S	D	F	I	T	180
496	AGT	GGT	GCT	GAT	TCT	GCT	TGG	TGT	CAA	ACA	TCA	GAT	TTC	ATC	ACA	540
181	V	A	W	L	I	F	L	C	V	V	L	C	G	S	S	195
541	GTC	GCG	TGG	CTG	ATT	TTT	TTA	TGT	GTG	GTT	CTC	TGT	GGG	TCC	AGC	585
196	L	V	L	L	I	R	I	L	C	G	S	R	K	I	P	210
586	CTG	GTC	CTG	CTG	ATC	AGG	ATT	CTC	TGT	GGA	TCC	CGG	AAG	ATA	CCG	630
211	L	T	R	L	Y	V	T	I	L	L	T	V	L	V	F	225
631	CTG	ACC	AGG	CTG	TAC	GTG	ACC	ATC	CTG	CTC	ACA	GTA	CTG	GTC	TTC	675
226	L	L	C	G	L	P	F	G	I	Q	F	F	L	F	L	240
676	CTC	CTC	TGT	GGC	CTG	CCC	TTT	GGC	ATT	CAG	TTT	TTC	CTA	TTT	TTA	720
241	W	I	H	V	D	R	E	V	L	F	C	H	V	H	L	255
721	TGG	ATC	CAC	GTG	GAC	AGG	GAA	GTC	TTA	TTT	TGT	CAT	GTT	CAT	CTA	765
256	V	S	I	F	L	S	A	L	N	S	S	A	N	P	I	270

271	I	Y	F	F	V	G	S	F	R	Q	R	Q	N	R	Q	285
811	ATT	TAC	TTC	TTC	GTG	GGC	TCC	TTT	AGG	CAG	CGT	CAA	AAT	AGG	CAG	855
286	N	L	K	L	V	L	Q	R	A	L	Q	D	A	S	E	300
856	AAC	CTG	AAG	CTG	GTT	CTC	CAG	AGG	GCT	CTG	CAG	GAC	GCG	TCT	GAG	900
301	V	D	E	G	G	G	Q	L	P	E	E	I	L	E	L	315
901	GTG	GAT	GAA	GGT	GGA	GGG	CAG	CTT	CCT	GAG	GAA	ATC	CTG	GAG	CTG	945
316	S	G	S	R	L	E	Q	*								323
946	TCG	GGA	AGC	AGA	TTG	GAG	CAG	TGA								969

Amino acid sequence of human GPCR α 5 (322 amino acids) (SEQ ID NO:6). The seven predicted transmembrane domains are underlined.

MDPTISTLDTELTPINGTEETLCYKQTL~~SLTVLTCIVSLVGLTGNAVVLWLLGCRMRRNAFSIYILNLAAADFLFLSGRL~~
~~IYSLLSFISIPHTISKILYPVMMFSYFAGLSFLSAVSTERCLSVLWPIWYRCHRP~~THLSAVVCVLLWALSLLRSILEWML
 CGFLFSGADSAWCQTSDFITVAWLIFLCVVL~~CGSSLVLLIRILCGSRKIPLTRLYVTILLTVLVFLLCGLPFGIQFFLFL~~
 WIHVDREVL~~FCHVHLVSIFLSALNSSANPIIYFFVGSFRQRQNRQNLKLVLQRALQDASEVDEGGGQLPEEILELSGSRL~~
 EQ

At the amino acid sequence level, the human GPCR α 5 is 31% identical to the human mas receptor.

Nucleotide and deduced amino acid sequence of human GPCR α 7 (SEQ ID NO: 7 and 8 respectively)

1	M	N	Q	T	L	N	S	S	G	T	V	E	S	A	L	15
1	ATG	AAC	CAG	ACT	TTG	AAT	AGC	AGT	GGG	ACC	GTG	GAG	TCA	GCC	CTA	45
16	N	Y	S	R	G	S	T	V	H	T	A	Y	L	V	L	30
46	AAC	TAT	TCC	AGA	GGG	AGC	ACA	GTG	CAC	ACG	GCC	TAC	CTG	GTG	CTG	90
31	S	S	L	A	M	F	T	C	L	C	G	M	A	G	N	45
91	AGC	TCC	CTG	GCC	ATG	TTC	ACC	TGC	CTG	TGC	GGG	ATG	GCA	GGC	AAC	135
46	S	M	V	I	W	L	L	G	F	R	M	H	R	N	P	60
136	AGC	ATG	GTG	ATC	TGG	CTG	CTG	GGC	TTT	CGA	ATG	CAC	AGG	AAC	CCC	180
61	F	C	I	Y	I	L	N	L	A	A	A	D	L	L	F	75
181	TTC	TGC	ATC	TAT	ATC	CTC	AAC	CTG	GCG	GCA	GCC	GAC	CTC	CTC	TTC	225
76	L	F	S	M	A	S	T	L	S	L	E	T	Q	P	L	90
226	CTC	TTC	AGC	ATG	GCT	TCC	ACG	CTC	AGC	CTG	GAA	ACC	CAG	CCC	CTG	270
91	V	N	T	T	D	K	V	H	E	L	M	K	R	L	M	105
271	GTC	AAT	ACC	ACT	GAC	AAG	GTC	CAC	GAG	CTG	ATG	AAG	AGA	CTG	ATG	315
106	Y	F	A	Y	T	V	G	L	S	L	L	T	A	I	S	120
316	TAC	TTT	GCC	TAC	ACA	GTG	GGC	CTG	AGC	CTG	CTG	ACG	GCC	ATC	AGC	360
121	T	Q	R	C	L	S	V	L	F	P	I	W	F	K	C	135
361	ACC	CAG	CGC	TGT	CTC	TCT	GTC	CTC	TTC	CCT	ATC	TGG	TTC	AAG	TGT	405
136	H	R	P	R	H	L	S	A	W	V	C	G	L	L	W	150
406	CAC	CGG	CCC	AGG	CAC	CTG	TCA	GCC	TGG	GTG	TGT	GGC	CTG	CTG	TGG	450
151	T	L	C	L	L	M	N	G	L	T	S	S	F	C	S	165
451	ACA	CTC	TGT	CTC	CTG	ATG	AAC	GGG	TTG	ACC	TCT	TCC	TTC	TGC	AGC	495
166	K	F	L	K	F	N	E	D	R	C	F	R	V	D	M	180
496	AAG	TTC	TTG	AAA	TTC	AAT	GAA	GAT	CGG	TGC	TTC	AGG	GTG	GAC	ATG	540
181	V	Q	A	A	L	I	M	G	V	L	T	P	V	M	T	195
541	GTC	CAG	GCC	GCC	CTC	ATC	ATG	GGG	GTC	TTA	ACC	CCA	GTG	ATG	ACT	585
196	L	S	S	L	T	L	F	V	W	V	R	R	S	S	Q	210
586	CTG	TCC	AGC	CTG	ACC	CTC	TTT	GTC	TGG	GTG	CGG	AGG	AGC	TCC	CAG	630
211	Q	W	R	R	Q	P	T	R	L	F	V	V	V	L	A	225
631	CAG	TGG	CGG	CGG	CAG	CCC	ACA	CGG	CTG	TTC	GTG	GTG	GTC	CTG	GCC	675
226	S	V	L	V	F	L	I	C	S	L	P	L	S	I	Y	240
676	TCT	GTC	CTG	GTG	TTC	CTC	ATC	TGT	TCC	CTG	CCT	CTG	AGC	ATC	TAC	720
241	W	F	V	L	Y	W	L	S	L	P	P	E	M	Q	V	255
721	TGG	TTT	GTG	CTC	TAC	TGG	TTG	AGC	CTG	CCG	CCC	GAG	ATG	CAG	GTC	765

271	A	N	P	V	I	Y	F	L	V	G	S	R	R	S	H	285
811	GCC	AAC	CCC	GTC	ATC	TAC	TTC	CTG	GTG	GGC	AGC	CGG	AGG	AGC	CAC	855
286	R	L	P	T	R	S	L	G	T	V	L	Q	Q	A	L	300
856	AGG	CTG	CCC	ACC	AGG	TCC	CTG	GGG	ACT	GTG	CTC	CAA	CAG	GCG	CTT	900
301	R	E	E	P	E	L	E	G	G	E	T	P	T	V	G	315
901	CGC	GAG	GAG	CCC	GAG	CTG	GAA	GGT	GGG	GAG	ACG	CCC	ACC	GTG	GGC	945
316	T	N	E	M	G	A	*									322
946	ACC	AAT	GAG	ATG	GGG	GCT	TGA									966

Amino acid sequence of human GPCR α 7 (321 amino acids) (SEQ ID NO:8). The seven predicted transmembrane domains are underlined.

MNQTLNSSGTVESALNYSRGSTVHTAYLVLSLAMFTCLCGMAGNSMVIWLLGFRMHRNPFCIYILNLAAADLLFLFSMA
STLSLETQPLVNTTDKVHELMKRLMYFAYTVGLSLLTAISTQRCLSVLFPIWfKCHRPRLSAWVCGLLWTLCLLMNGLT
SSFCSKFLKFNEDRCFRVDMVQAALIMGVLT PVM TLSSLTLFVWVRSSQWRRQPTRLFVVVLASVLVFLICSLPLSIY
WFLYWLSPPEMQVLCFSL SRLSSSVSSSANPVIYFLVGSRRSHRLPTRSLGTVLQQALREEPELEGGETPTVGTNEMG
A

At the amino acid sequence level, the human GPCR α 7 is 29% identical to the rat RTA receptor.

Nucleotide and deduced amino acid sequence of human GPCR α 9 (SEQ ID NO: 9 and 10 respectively)

1	M	E	A	D	L	G	A	T	G	H	R	P	R	T	E	15
1	ATG	GAA	GCT	GAC	CTG	GGT	GCC	ACT	GGC	CAC	AGG	CCC	CGC	ACA	GAG	45
16	L	D	D	E	D	S	Y	P	Q	G	G	W	D	T	V	30
46	CTT	GAT	GAT	GAG	GAC	TCC	TAC	CCC	CAA	GGT	GGC	TGG	GAC	ACG	GTC	90
31	F	L	V	A	L	L	L	L	G	L	P	A	N	G	L	45
91	TTC	CTG	GTG	GCC	CTG	CTG	CTC	CTT	GGG	CTG	CCA	GCC	AAT	GGG	TTG	135
46	M	A	W	L	A	G	S	Q	A	R	H	G	A	G	T	60
136	ATG	GCG	TGG	CTG	GCC	GGC	TCC	CAG	GCC	CGG	CAT	GGA	GCT	GGC	ACG	180
61	R	L	A	L	L	L	L	S	L	A	L	S	D	F	L	75
181	CGT	CTG	GCG	CTG	CTC	CTG	CTC	AGC	CTG	GCC	CTC	TCT	GAC	TTC	TTG	225
76	F	L	A	A	A	A	F	Q	I	L	E	I	R	H	G	90
226	TTC	CTG	GCA	GCA	GCG	GCC	TTC	CAG	ATC	CTA	GAG	ATC	CGG	CAT	GGG	270
91	G	H	W	P	L	G	T	A	A	C	R	F	Y	Y	F	105
271	GGA	CAC	TGG	CCG	CTG	GGG	ACA	GCT	GCC	TGC	CGC	TTC	TAC	TAC	TTC	315
106	L	W	G	V	S	Y	S	S	G	L	F	L	L	A	A	120
316	CTA	TGG	GGC	GTG	TCC	TAC	TCC	TCC	GGC	CTC	TTC	CTG	CTG	GCC	GCC	360
121	L	S	L	D	R	C	L	L	A	L	C	P	H	W	Y	135
361	CTC	AGC	CTC	GAC	CGC	TGC	CTG	CTG	GCG	CTG	TGC	CCA	CAC	TGG	TAC	405
136	P	G	H	R	P	V	R	L	P	L	W	V	C	A	G	150
406	CCT	GGG	CAC	CGC	CCA	GTC	CGC	CTG	CCC	CTC	TGG	GTC	TGC	GCC	GGT	450
151	V	W	V	L	A	T	L	F	S	V	P	W	L	V	F	165
451	GTC	TGG	GTG	CTG	GCC	ACA	CTC	TTC	AGC	GTG	CCC	TGG	CTG	GTC	TTC	495
166	P	E	A	A	V	W	W	Y	D	L	V	I	C	L	D	180
496	CCC	GAG	GCT	GCC	GTC	TGG	TGG	TAC	GAC	CTG	GTC	ATC	TGC	CTG	GAC	540
181	F	W	D	S	E	E	L	S	L	R	M	L	E	V	L	195
541	TTC	TGG	GAC	AGC	GAG	GAG	CTG	TCG	CTG	AGG	ATG	CTG	GAG	GTC	CTG	585
196	G	G	F	L	P	F	L	L	L	L	V	C	H	V	L	210
586	GGG	GGC	TTC	CTG	CCT	TTC	CTC	CTG	CTG	CTC	GTC	TGC	CAC	GTG	CTC	630
211	T	Q	A	T	A	C	R	T	C	H	R	Q	Q	Q	P	225
631	ACC	CAG	GCC	ACA	GCC	TGT	CGC	ACC	TGC	CAC	CGC	CAA	CAG	CAG	CCC	675
226	A	A	C	R	G	F	A	R	V	A	R	T	I	L	S	240
676	GCA	GCC	TGC	CGG	GGC	TTC	GCC	CGT	GTG	GCC	AGG	ACC	ATT	CTG	TCA	720
241	A	Y	V	V	L	R	L	P	Y	Q	L	A	Q	L	L	255
721	GCC	TAT	GTG	GTC	CTG	AGG	CTG	CCC	TAC	CAG	CTG	GCC	CAG	CTG	CTC	765
256	Y	L	A	F	L	W	D	V	Y	S	G	Y	L	L	W	270

271	E	A	L	V	Y	S	D	Y	L	I	L	L	N	S	C	285
811	GAG	GCC	CTG	GTC	TAC	TCC	GAC	TAC	CTG	ATC	CTA	CTC	AAC	AGC	TGC	855
286	L	S	P	F	L	C	L	M	A	S	A	D	L	R	T	300
856	CTC	AGC	CCC	TTC	CTC	TGC	CTC	ATG	GCC	AGT	GCC	GAC	CTC	CGG	ACC	900
301	L	L	R	S	V	L	S	S	F	A	A	A	L	C	E	315
901	CTG	CTG	CGC	TCC	GTG	CTC	TCC	TTC	GCG	GCA	GCT	CTC	TGC	GAG		945
316	E	R	P	G	S	F	T	P	T	E	P	Q	T	Q	L	330
946	GAG	CGG	CCG	GGC	AGC	TTC	ACG	CCC	ACT	GAG	CCA	CAG	ACC	CAG	CTA	990
331	D	S	E	G	P	T	L	P	E	P	M	A	E	A	Q	345
991	GAT	TCT	GAG	GGT	CCA	ACT	CTG	CCA	GAG	CCG	ATG	GCA	GAG	GCC	CAG	1035
346	S	Q	M	D	P	V	A	Q	P	Q	V	N	P	T	L	360
1036	TCA	CAG	ATG	GAT	CCT	GTG	GCC	CAG	CCT	CAG	GTG	AAC	CCC	ACA	CTC	1080
361	Q	P	R	S	D	P	T	A	Q	P	Q	L	N	P	T	375
1081	CAG	CCA	CGA	TCG	GAT	CCC	ACA	GCT	CAG	CCA	CAG	CTG	AAC	CCT	ACG	1125
376	A	Q	P	Q	S	D	P	T	A	Q	P	Q	L	N	L	390
1126	GCC	CAG	CCA	CAG	TCG	GAT	CCC	ACA	GCC	CAG	CCA	CAG	CTG	AAC	CTC	1170
391	M	A	Q	P	Q	S	D	S	V	A	Q	P	Q	A	D	405
1171	ATG	GCC	CAG	CCA	CAG	TCA	GAT	TCT	GTG	GCC	CAG	CCA	CAG	GCA	GAC	1215
406	T	N	V	Q	T	P	A	P	A	A	S	S	V	P	S	420
1216	ACT	AAC	GTC	CAG	ACC	CCT	GCA	CCT	GCT	GCC	AGT	TCT	GTG	CCC	AGT	1260
421	P	C	D	E	A	S	P	T	P	S	S	H	P	T	P	435
1261	CCC	TGT	GAT	GAA	GCT	TCC	CCA	ACC	CCA	TCC	TCG	CAT	CCT	ACC	CCA	1305
436	G	A	L	E	D	P	A	T	P	P	A	S	E	G	E	450
1306	GGG	GCC	CTT	GAG	GAC	CCA	GCC	ACA	CCT	CCT	GCC	TCT	GAA	GGA	GAA	1350
451	S	P	S	S	T	P	P	E	A	A	P	G	A	G	P	465
1351	AGC	CCC	AGC	AGC	ACC	CCG	CCA	GAG	GCG	GCC	CCG	GGC	GCA	GGC	CCC	1395
466	T	*														467
1396	ACG	TGA														1401

Amino acid sequence of human GPCR α 9 (466 amino acids) (SEQ ID NO:10). The six predicted transmembrane domains are underlined.

MEADLGATGHRPRT~~ELDD~~EDSY~~PQGGWDTVFLVAL~~LLLLGLPANG~~LM~~AWLAGSQARHGAGTRLA~~LLLLSL~~ALSDFLFLAAA
 AFQILEIRHGGHWPLGTAACRFYYFLWGSYSSGLFLLAALS~~SLDRCLLALCPHWYPGHRPVRLPLWVCAGVWVLATLFSV~~
 PWLVFPEAAVWYDLVICLDFWDSEELSLRMLEVLGGFLPFL~~LLLLVCHVLTQATACRTCH~~RQQQPAACRGFARVARTILS
 AYVVLRLPYQLAQLLYLAFLWDVYSGYLLWEALVYSDYLILLNSCLSPFLCLMASADLRTLLRSVLSSFAAALCEERP
 FGPSTPQQLDSEGPTLPEPMAEAQSQMDPVAQPVNPTLQPRSDPTAQPOLNPTAQPSDPTAQPOLNLMAQPSDSVA
 QPQADTNVQTAPAAASSVSPCDEASPTPSSHPTPGALEDPATPPASEGESPSSTPPEAAPGAGPT

At the amino acid sequence level, the human GPCR α 9 is 33% identical to the human ChemR23 receptor.

Nucleotide and deduced amino acid sequence of human GPCR α 14 (SEQ ID NO: 11 and 12 respectively)

1	M	Y	N	G	S	C	C	R	I	E	G	D	T	I	S	15
1	ATG	TAC	AAC	GGG	TCG	TGC	TGC	CGC	ATC	GAG	GGG	GAC	ACC	ATC	TCC	45
16	Q	V	M	P	P	L	L	I	V	A	F	V	L	G	A	30
46	CAG	GTG	ATG	CCG	CCG	CTG	CTC	ATT	GTG	GCC	TTT	GTG	CTG	GGC	GCA	90
31	L	G	N	G	V	A	L	C	G	F	C	F	H	M	K	45
91	CTA	GGC	AAT	GGG	GTC	GCC	CTG	TGT	GGT	TTC	TGC	TTC	CAC	ATG	AAG	135
46	T	W	K	P	S	T	V	Y	L	F	N	L	A	V	A	60
136	ACC	TGG	AAG	CCC	AGC	ACT	GTT	TAC	CTT	TTC	AAT	TTG	GCC	GTG	GCT	180
61	D	F	L	L	M	I	C	L	P	F	R	T	D	Y	Y	75
181	GAT	TTC	CTC	CTT	ATG	ATC	TGC	CTG	CCT	TTT	CGG	ACA	GAC	TAT	TAC	225
76	L	R	R	R	H	W	A	F	G	D	I	P	C	R	V	90
226	CTC	AGA	CGT	AGA	CAC	TGG	GCT	TTT	GGG	GAC	ATT	CCC	TGC	CGA	GTG	270
91	G	L	F	T	L	A	M	N	R	A	G	S	I	V	F	105
271	GGG	CTC	TTC	ACG	TTG	GCC	ATG	AAC	AGG	GCC	GGG	AGC	ATC	GTG	TTC	315
106	L	T	V	V	A	A	D	R	Y	F	K	V	V	H	P	120
316	CTT	ACG	GTG	GTG	GCT	GCG	GAC	AGG	TAT	TTC	AAA	GTG	GTC	CAC	CCC	360
121	H	H	A	V	N	T	I	S	T	R	V	A	A	G	I	135
361	CAC	CAC	GCG	GTG	AAC	ACT	ATC	TCC	ACC	CGG	GTG	GCG	GCT	GGC	ATC	405
136	V	C	T	L	W	A	L	V	I	L	G	T	V	Y	L	150
406	GTC	TGC	ACC	CTG	TGG	GCC	CTG	GTC	ATC	CTG	GGA	ACA	GTG	TAT	CTT	450
151	L	L	E	N	H	L	C	V	Q	E	T	A	V	S	C	165
451	TTG	CTG	GAG	AAC	CAT	CTC	TGC	GTG	CAA	GAG	ACG	GCC	GTC	TCC	TGT	495
166	E	S	F	I	M	E	S	A	N	G	W	H	D	I	M	180
496	GAG	AGC	TTC	ATC	ATG	GAG	TCG	GCC	AAT	GGC	TGG	CAT	GAC	ATC	ATG	540
181	F	Q	L	E	F	F	M	P	L	G	I	I	L	F	C	195
541	TTC	CAG	CTG	GAG	TTC	TTT	ATG	CCC	CTC	GGC	ATC	ATC	TTA	TTT	TGC	585
196	S	F	K	I	V	W	S	L	R	R	R	Q	Q	L	A	210
586	TCC	TTC	AAG	ATT	GTT	TGG	AGC	CTG	AGG	CGG	AGG	CAG	CAG	CTG	GCC	630
211	R	Q	A	R	M	K	K	A	T	R	F	I	M	V	V	225
631	AGA	CAG	GCT	CGG	ATG	AAG	AAG	GCG	ACC	CGG	TTC	ATC	ATG	GTG	GTG	675
226	A	I	V	F	I	T	C	Y	L	P	S	V	S	A	R	240
676	GCA	ATT	GTG	TTC	ATC	ACA	TGC	TAC	CTG	CCC	AGC	GTG	TCT	GCT	AGA	720
241	L	Y	F	L	W	T	V	P	S	S	A	C	D	P	S	255
721	CTC	TAT	TTC	CTC	TGG	ACG	GTG	CCC	TCG	AGT	GCC	TGC	GAT	CCC	TCT	765

271	S	M	L	D	P	L	V	Y	Y	F	S	S	P	S	F	285
811	AGC	ATG	CTG	GAT	CCC	CTG	GTG	TAT	TAT	TTT	TCA	AGC	CCC	TCC	TTT	855
286	P	K	F	Y	N	K	L	K	I	C	S	L	K	P	K	300
856	CCC	AAA	TTC	TAC	AAC	AAG	CTC	AAA	ATC	TGC	AGT	CTG	AAA	CCC	AAG	900
301	Q	P	G	H	S	K	T	Q	R	P	E	E	M	P	I	315
901	CAG	CCA	GGA	CAC	TCA	AAA	ACA	CAA	AGG	CCG	GAA	GAG	ATG	CCA	ATT	945
316	S	N	L	G	R	R	S	C	I	S	V	A	N	S	F	330
946	TCG	AAC	CTC	GGT	CGC	AGG	AGT	TGC	ATC	AGT	GTG	GCA	AAT	AGT	TTC	990
331	Q	S	Q	S	D	G	Q	W	D	P	H	I	V	E	W	345
991	CAA	AGC	CAG	TCT	GAT	GGG	CAA	TGG	GAT	CCC	CAC	ATT	GTT	GAG	TGG	1035
346	H	*														347
1036	CAC	TGA														1041

Amino acid sequence of human GPCR α 14 (346 amino acids) (SEQ ID NO:12). The seven predicted transmembrane domaines are underlined.

MYNGSCCRIEGDTISQVMPPLLI~~VAFVLGALGNGVALCGFCFHMKTWKPSTVYLFNLAVADFLLMICLPFRTDYLR~~RRH
WAFGDIPCRVGLFTLAMNRAGSIVFLTVVAADRYFKVVHPH~~AVNTISTRVAAGIVCTLWALVILGT~~VYLLLENHLCVQE
TAVSCSFIMESANGWHDIMFQLEFFMPLGIILFCSFKIVWSLRRRQQLARQARMKKATRFIMVVAIVFITCYLPSVSAR
LYFLWTVPSSACDPSVHGALHITLSFTYMNSMLDPLVYYFSSPSFPKFYNKLKICSLKPKQPGH~~SKTQRPEEMPISNLGR~~
RSCISVANSFQSQSDGQWDPHIVEWH

At the amino acid sequence level, the human GPCR α 14 is 50% identical to the human HM74 receptor.

Nucleotide and deduced amino acid sequence of human GPCR α 16 (SEQ ID NO: 13 and 14 respectively). This nucleotide sequence is located on the chromosome 4.

1	M	G	P	G	E	A	L	L	A	G	L	L	V	M	V	15
1	ATG	GGC	CCC	GGC	GAG	GCG	CTG	CTG	GCG	GGT	CTC	CTG	GTG	ATG	GTA	45
16	L	A	V	A	L	L	S	N	A	L	V	L	L	C	C	30
46	CTG	GCC	GTG	GCG	CTG	CTA	TCC	AAC	GCA	CTG	GTG	CTG	CTT	TGT	TGC	90
31	A	Y	S	A	E	L	R	T	R	A	S	G	V	L	L	45
91	GCC	TAC	AGC	GCT	GAG	CTC	CGC	ACT	CGA	GCC	TCA	GGC	GTC	CTC	CTG	135
46	V	N	L	S	L	G	H	L	L	L	A	A	L	D	M	60
136	GTG	AAT	CTG	TCT	CTG	GGC	CAC	CTG	CTG	CTG	GCG	GCG	CTG	GAC	ATG	180
61	P	F	T	L	L	G	V	M	R	G	R	T	P	S	A	75
181	CCC	TTC	ACG	CTG	CTC	GGT	GTG	ATG	CGC	GGG	CGG	ACA	CCG	TCG	GCG	225
76	P	G	A	C	Q	V	I	G	F	L	D	T	F	L	A	90
226	CCC	GGC	GCA	TGC	CAA	GTC	ATT	GGC	TTC	CTG	GAC	ACC	TTC	CTG	GCG	270
91	S	N	A	A	L	S	V	A	A	L	S	A	D	Q	W	105
271	TCC	AAC	GCG	GCG	CTG	AGC	GTG	GCG	GCG	CTG	AGC	GCA	GAC	CAG	TGG	315
106	L	A	V	G	F	P	L	R	Y	A	G	R	L	R	P	120
316	CTG	GCA	GTG	GGC	TTC	CCA	CTG	CGC	TAC	GCC	GGA	CGC	CTG	CGA	CCG	360
121	R	Y	A	G	L	L	L	G	C	A	W	G	Q	S	L	135
361	CGC	TAT	GCC	GGC	CTG	CTG	CTG	GGC	TGT	GCC	TGG	GGA	CAG	TCG	CTG	405
136	A	F	S	G	A	A	L	G	C	S	W	L	G	Y	S	150
406	GCC	TTC	TCA	GGC	GCT	GCA	CTT	GGC	TGC	TCG	TGG	CTT	GGC	TAC	AGC	450
151	S	A	F	A	S	C	S	L	R	L	P	P	E	P	E	165
451	AGC	GCC	TTC	GCG	TCC	TGT	TCG	CTG	CGC	CTG	CCG	CCC	GAG	CCT	GAG	495
166	R	P	R	F	A	A	F	T	A	T	L	H	A	V	G	180
496	CGT	CCG	CGC	TTC	GCA	GCC	TTC	ACC	GCC	ACG	CTC	CAT	GCC	GTG	GGC	540
181	F	V	L	P	L	A	V	L	C	L	T	S	L	Q	V	195
541	TTC	GTG	CTG	CCG	CTG	GCG	GTG	CTC	TGC	CTC	ACC	TCG	CTC	CAG	GTG	585
196	H	R	V	A	R	R	H	C	Q	R	M	D	T	V	T	210
586	CAC	CGG	GTG	GCA	CGC	AGA	CAC	TGC	CAG	CGC	ATG	GAC	ACC	GTC	ACC	630
211	M	K	A	L	A	L	L	A	D	L	H	P	R	Y	W	225
631	ATG	AAG	GCG	CTC	GCG	CTG	CTC	GCC	GAC	CTG	CAC	CCC	AGG	TAT	TGG	675
226	P	S	A	C	R	Q	A	Q	A	R	D	L	G	A	P	240
676	CCC	AGT	GCA	TGC	CGA	CAG	GCC	CAG	GCC	AGG	GAC	TTG	GGC	GCT	CCC	720
241	W	A	V	G	L	R	S	L	W	A	S	P	P	L	L	255
721	TGG	GCA	GTT	GGC	TTG	AGG	AGC	CTG	TGG	GCA	TCA	CCA	CCG	TTA	CTC	765
256	C	P	E	F	T	S	H	S	T	A	P	A	R	C	S	270

271	Q	G	F	P	V	G	S	L	V	Q	T	L	R	G	P	285
811	CAG	GGG	TTT	CCT	GTT	GGT	TCA	TTG	GTG	CAG	ACA	CTG	CGG	GGG	CCT	855
286	L	P	P	G	I	C	A	H	S	A	Q	G	A	L	R	300
856	CTG	CCT	CCT	GGG	ATA	TGT	GCT	CAC	AGT	GCA	CAG	GGA	GCT	TTG	CGC	900
301	R	A	V	G	C	A	S	P	G	G	V	P	R	A	L	315
901	AGA	GCT	GTG	GGG	TGT	GCT	TCT	CCG	GGA	GGG	GTT	CCG	CGG	GCT	CTG	945
316	L	W	A	A	R	H	T	P	P	V	H	G	C	G	S	330
946	CTG	TGG	GCG	GCC	AGA	CAC	ACC	CCT	CCT	GTG	CAT	GGC	TGT	GGG	TCT	990
331	E	A	S	A	C	F	C	P	L	L	T	Q	C	P	C	345
991	GAG	GCA	TCT	GCT	TGT	TTC	TGC	CCA	CTG	CTG	ACC	CAG	TGC	CCT	TGC	1035
346	M	D	L	G	F	K	S	*								352
1036	ATG	GAC	TTG	GGC	TTC	AAG	TCT	TGA								1059

Amino acid sequence of human GPCR α 16 (352 amino acids) (SEQ ID NO: 14). The six predicted transmembrane domains are underlined.

MGPGEALLAGLLVMVLAVALLSNALVLLCCAYSAELRTRASGVLLVNLSSLGHLLLAALDMPFTLLGVMRGRTPSAPGACQ
VIGFLDTFLASNAALSVAALSADQWLAVGFPLRYAGRLRPRYAGLLLGCAWGQSLAFSGAALGCSWLGYSSAFASCSLRL
PPEPERPRFAAFTATLHAVGFVLPLAVLCLTSLQVHRVARRHCQRMDTVTMKALALLADLHPRYWPSACRQAQARDLGAP
WAVGLRSLWASPPLLCPEFTSHSTAPARCSQGFPVGSLVQTLRGPLPPGICAHSAQGALRRAVGCASPGGVPRALLWAAR
HTPPVHGCSEASACFCPLLTQCPCMDLGFKS

At the amino acid sequence level, the human GPCR α 16 is 50% identical to the rat GPR 26 receptor.

Nucleotide and deduced amino acid sequence of human GPCR α 17 (SEQ ID NO: 15 and 16 respectively). This nucleotide sequence is located on the chromosome 2.

1	M	T	P	N	S	T	G	E	V	P	S	P	I	P	K	15
1	ATG	ACG	CCC	AAC	AGC	ACT	GGC	GAG	GTG	CCC	AGC	CCC	ATT	CCC	AAG	45
16	G	A	L	G	L	S	L	A	L	A	S	L	I	I	T	30
46	GGG	GCT	TTG	GGG	CTC	TCC	CTG	GCC	CTG	GCA	AGC	CTC	ATC	ATC	ACC	90
31	A	N	L	L	L	A	L	G	I	A	G	T	A	A	C	45
91	GCG	AAC	CTG	CTC	CTA	GCC	CTG	GGC	ATC	GCT	GGG	ACC	GCC	GCC	TGC	135
46	A	A	T	C	W	L	L	L	P	B	P	T	A	G	W	60
136	GCA	GCC	ACC	TGC	TGG	CTG	CTT	CTT	CCT	GAG	CCT	ACT	GCT	GGC	TGG	180
61	A	A	H	G	S	G	I	A	T	L	P	G	L	W	N	75
181	GCT	GCT	CAC	GGG	TCT	GGC	ATT	GCC	ACA	TTG	CCA	GGG	CTG	TGG	AAC	225
76	Q	S	R	R	G	Y	W	S	C	L	L	V	Y	L	A	90
226	CAG	AGT	CGC	CGG	GGT	TAC	TGG	TCC	TGC	CTC	CTC	GTC	TAC	TTG	GCT	270
91	P	N	F	S	F	L	S	L	L	A	N	L	L	L	V	105
271	CCC	AAC	TTC	TCC	TTC	CTC	TCC	CTG	CTT	GCC	AAC	CTC	TTG	CTG	GTG	315
106	H	G	E	R	Y	M	A	V	L	R	P	L	Q	P	P	120
316	CAC	GGG	GAG	CGC	TAC	ATG	GCA	GTC	CTG	AGG	CCA	CTC	CAG	CCC	CCT	360
121	G	S	I	R	L	A	L	L	L	T	W	A	G	P	L	135
361	GGG	AGC	ATT	CGG	CTG	GCC	CTG	CTC	CTC	ACC	TGG	GCT	GGT	CCC	CTG	405
136	L	F	A	S	L	P	A	L	G	W	N	H	W	T	P	150
406	CTC	TTT	GCC	AGT	CTG	CCC	GCT	CTG	GGG	TGG	AAC	CAC	TGG	ACC	CCT	450
151	G	A	N	C	S	S	Q	A	I	F	P	A	P	Y	L	165
451	GGT	GCC	AAC	TGC	AGC	TCC	CAG	GCT	ATC	TTC	CCA	GCC	CCC	TAC	CTG	495
166	Y	L	E	V	Y	G	L	L	L	P	A	V	G	A	A	180
496	TAC	CTC	GAA	GTC	TAT	GGG	CTC	CTG	CTG	CCC	GCC	GTG	GGT	GCT	GCT	540
181	A	F	L	S	V	R	V	L	A	T	A	H	R	Q	L	195
541	GCC	TTC	CTC	TCT	GTC	CGC	GTG	CTG	GCC	ACT	GCC	CAC	CGC	CAG	CTG	585
196	Q	D	I	C	R	L	E	R	A	V	C	R	D	E	P	210
586	CAG	GAC	ATC	TGC	CGG	CTG	GAG	CGG	GCA	GTG	TGC	CGC	GAT	GAG	CCC	630
211	S	A	L	A	R	A	L	T	W	R	Q	A	R	A	Q	225
631	TCC	GCC	CTG	GCC	CGG	GCC	CTT	ACC	TGG	AGG	CAG	GCA	AGG	GCA	CAG	675
226	A	G	A	M	L	L	F	G	L	C	W	G	P	Y	V	240
676	GCT	GGA	GCC	ATG	CTG	CTC	TTC	GGG	CTG	TGC	TGG	GGG	CCC	TAC	GTG	720
241	A	T	L	L	L	S	V	L	A	Y	E	Q	R	P	P	255
721	GCC	ACA	CTG	CTC	CTC	TCA	GTC	CTG	GCC	TAT	GAG	CAG	CGC	CCG	CCA	765

271	S	A	A	A	V	P	V	A	M	G	L	G	D	Q	R	285
811	AGT	GCA	GCG	GCA	GTG	CCC	GTA	GCC	ATG	GGG	CTG	GGC	GAT	CAG	CGC	855
286	Y	T	A	P	W	R	Q	P	P	K	G	A	C	R	G	300
856	TAC	ACA	GCC	CCC	TGG	AGG	CAG	CCG	CCC	AAA	GGT	GCC	TGC	AGG	GGC	900
301	C	G	E	E	P	P	G	T	V	P	A	P	A	L	P	315
901	TGT	GGG	GAA	GAG	CCT	CCC	GGG	ACA	GTC	CCG	GCC	CCA	GCA	TTG	CCT	945
316	T	T	Q	A	A	K	A	V	S	T	W	T	*			327
946	ACC	ACC	CAA	GCA	GCC	AAA	GCA	GTG	TCG	ACC	TGG	ACT	TGA			984

Amino acid sequence of human GPCR α 17 (327 amino acids) (SEQ ID NO:16). The seven predicted transmembrane domains are underlined.

MTPNSTGEVPSPIPKGALGLSLALASLIITANLLLALGIAGTAACAATCWLLLPEPTAGWAAHGSGIATLPGLWNQSRRG
YWSCLLVYLAPNFSFLSLLANLLLVHGERYMAVLRPLQPPGSIRLALLLTWAGPLLFASLPALGWNHWPGANCSSQAIF
PAPYLYLEVYGLLLPAVGAAAFLSVRVLATAHRQLQDICRLERAVCRDEPSALARALTWRQARAQAGAMLLFGLCWGPYV
ATILLSVLAYEQRPPLGPGTLLSLLSLGSASAAAVPVAMCLCDQRYTAPWRQPPKGACRGCGEPPGTVPAPALPTTQAA
 KAVSTWT

At the amino acid sequence level, the human GPCR α 17 is 28% identical to the human EDG6 receptor

Nucleotide and deduced amino acid sequence of human GPCR α 18 (SEQ ID NO: 17 and 18 respectively). This nucleotide sequence is located on the chromosome 2.

1	M	G	D	E	L	A	P	C	P	V	G	T	T	A	W	15
1	ATG	GGG	GAT	GAG	CTG	GCA	CCT	TGC	CCT	GTG	GGC	ACT	ACA	GCT	TGG	45
16	P	A	L	I	Q	L	I	S	K	T	P	C	M	P	Q	30
46	CCG	GCC	CTG	ATC	CAG	CTC	ATC	AGC	AAG	ACA	CCC	TGC	ATG	CCC	CAA	90
31	A	A	S	N	T	S	L	G	L	G	D	L	R	V	P	45
91	GCA	GCC	AGC	AAC	ACT	TCC	TTG	GGC	CTG	GGG	GAC	CTC	AGG	GTG	CCC	135
46	S	S	M	L	Y	W	L	F	L	P	S	S	L	L	A	60
136	AGC	TCC	ATG	CTG	TAC	TGG	CTT	TTC	CTT	CCC	TCA	AGC	CTG	CTG	GCT	180
61	A	A	T	L	A	V	S	P	L	L	L	V	T	I	L	75
181	GCA	GCC	ACA	CTG	GCT	GTC	AGC	CCC	CTG	CTG	CTG	GTG	ACC	ATC	CTG	225
76	R	N	Q	R	L	R	Q	E	P	H	Y	L	L	P	A	90
226	CGG	AAC	CAA	CGG	CTG	CGA	CAG	GAG	CCC	CAC	TAC	CTG	CTC	CCG	GCT	270
91	N	I	L	L	S	D	L	A	Y	I	L	L	H	M	L	105
271	AAC	ATC	CTG	CTC	TCA	GAC	CTG	GCC	TAC	ATT	CTC	CTC	CAC	ATG	CTC	315
106	I	S	S	S	S	L	G	G	W	E	L	G	R	M	A	120
316	ATC	TCC	TCC	AGC	AGC	CTG	GGT	GGC	TGG	GAG	CTG	GGC	CGC	ATG	GCC	360
121	C	G	I	L	T	D	A	V	F	A	A	C	T	S	T	135
361	TGT	GGC	ATT	CTC	ACT	GAT	GCT	GTC	TTC	GCC	GCC	TGC	ACC	AGC	ACC	405
136	I	L	S	F	T	A	I	V	L	H	T	Y	L	A	V	150
406	ATC	CTG	TCC	TTC	ACC	GCC	ATT	GTG	CTG	CAC	ACC	TAC	CTG	GCA	GTC	450
151	I	H	P	L	R	Y	L	S	F	M	S	H	G	A	A	165
451	ATC	CAT	CCA	CTG	CGC	TAC	CTC	TCC	TTC	ATG	TCC	CAT	GGG	GCT	GCC	495
166	W	K	A	V	A	L	I	W	L	V	A	C	C	F	P	180
496	TGG	AAG	GCA	GTG	GCC	CTC	ATC	TGG	CTG	GTG	GCC	TGC	TGC	TTC	CCC	540
181	T	F	L	I	W	L	S	K	W	Q	D	A	Q	L	E	195
541	ACA	TTC	CTT	ATT	TGG	CTC	AGC	AAG	TGG	CAG	GAT	GCC	CAG	CTG	GAG	585
196	E	Q	G	A	S	Y	I	L	P	P	S	M	G	T	Q	210
586	GAG	CAA	GGA	GCT	TCA	TAC	ATC	CTA	CCA	CCA	AGC	ATG	GGC	ACC	CAG	630
211	P	G	C	G	L	L	V	I	V	T	Y	T	S	I	L	225
631	CCG	GGA	TGT	GGC	CTC	CTG	GTC	ATT	GTT	ACC	TAC	ACC	TCC	ATT	CTG	675
226	C	V	L	F	L	C	T	A	L	I	A	N	C	F	W	240
676	TGC	GTT	CTG	TTC	CTC	TGC	ACA	GCT	CTC	ATT	GCC	AAC	TGT	TTC	TGG	720
241	R	I	Y	A	E	A	K	T	S	G	I	W	G	Q	G	255
721	AGG	ATC	TAT	GCA	GAG	GCC	AAG	ACT	TCA	GGC	ATC	TGG	GGG	CAG	GGC	765

271	T	L	Y	V	S	T	G	V	V	F	S	L	D	M	V	285
811	ACA	TTG	TAC	GTG	AGC	ACA	GGG	GTG	GTG	TTC	TCC	CTG	GAC	ATG	GTG	855
286	L	T	R	Y	H	H	I	D	S	G	T	H	T	W	L	300
856	CTG	ACC	AGG	TAC	CAC	CAC	ATT	GAC	TCT	GGG	ACT	CAC	ACA	TGG	CTC	900
301	L	A	A	N	S	E	V	L	M	M	L	P	R	A	M	315
901	CTG	GCA	GCT	AAC	AGT	GAG	GTA	CTC	ATG	ATG	CTT	CCC	CGT	GCC	ATG	945
316	L	T	Y	L	Y	L	L	R	Y	R	Q	L	L	G	M	330
946	CTC	ACA	TAC	CTG	TAC	CTG	CTC	CGC	TAC	CGG	CAG	CTG	TTG	GGC	ATG	990
331	V	R	G	H	L	P	S	R	R	H	Q	A	I	F	T	345
991	GTC	CGG	GGC	CAC	CTC	CCA	TCC	AGG	AGG	CAC	CAG	GCC	ATC	TTT	ACC	1035
346	I	S	*													347
1036	ATT	TCC	TAG													1044

Amino acid sequence of human GPCR α 18 (347 amino acids) (SEQ ID NO:18). The seven predicted transmembrane domains are underlined.

MGDELAPCPVGTTAWPALIQISKTPCMPQAASNTSLGLGDLRVPSSMLYWLFLPSSLLAAATLAVSPLLLVTILRNQRL
 RQEPHYLLPANILLSDLAYILLHMLISSSSSLGGWELGRMACGILTDAVF~~AACTSTILSFTAIVLHTYLAVIHPLRYLSFM~~
 SHGA~~AWKAVALIWL~~VACCFPTFLIWLSKWQDAQLEEQGASYILPPSMGTQPGCGLLVIVITYTSILCVLFLCTALIANCFW
 RIYAEAKTSGIWGQGYSRARGTLLI~~HSVLITLYVSTGVVFS~~LD~~MVLTRYHHIDSGTHTWLLA~~ANSEVL~~MMLPRAM~~LT~~YLY~~
 LLRYRQLLGMVRGHLPSRRHQ~~AIFTIS~~

At the amino acid sequence level, the human GPCR α 18 is 25% identical to the rabbit 5HT $_{1D}$ - β receptor.

Nucleotide and deduced amino acid sequence (partial sequence) of human GPCR \times 19 (SEQ ID NO: 19 and 20 respectively). This nucleotide sequence is located on the chromosome 16.

1	G	P	H	R	S	Q	R	S	H	L	C	F	R	A	K	15
1	GGC	CCC	CAT	AGG	AGC	CAA	CGA	AGT	CAT	CTT	TGC	TTC	AGA	GCT	AAA	45
16	P	V	F	L	L	S	T	A	N	I	L	T	V	I	I	30
46	CCA	GTT	TTT	CTT	CTC	TCC	ACA	GCA	AAT	ATC	TTG	ACA	GTG	ATC	ATC	90
31	L	S	Q	L	V	A	R	R	Q	K	S	S	Y	N	Y	45
91	CTC	TCC	CAG	CTG	GTG	GCA	AGA	AGA	CAG	AAG	TCC	TCC	TAC	AAC	TAT	135
46	L	L	A	L	A	A	A	D	I	L	V	L	F	F	I	60
136	CTC	TTG	GCA	CTC	GCT	GCT	GCC	GAC	ATC	TTG	GTC	CTC	TTT	TTC	ATA	180
61	V	F	V	D	F	L	L	E	D	F	I	L	N	M	Q	75
181	GTG	TTT	GTG	GAC	TTC	CTG	TTG	GAA	GAT	TTC	ATC	TTG	AAC	ATG	CAG	225
76	M	P	Q	V	P	D	K	I	I	E	V	L	E	F	S	90
226	ATG	CCT	CAG	GTC	CCC	GAC	AAG	ATC	ATA	GAA	GTG	CTC	GAA	TTC	TCA	270
91	S	I	H	T	S	I	W	I	T	V	P	L	T	I	D	105
271	TCC	ATC	CAC	ACC	TCC	ATA	TGG	ATT	ACT	GTA	CCG	TTA	ACC	ATT	GAC	315
106	R	Y	I	A	V	C	H	P	L	K	Y	H	T	V	S	120
316	AGG	TAT	ATC	GCT	GTC	TGC	CAC	CCG	CTC	AAG	TAC	CAC	ACG	GTC	TCA	360
121	Y	P	A	R	T	R	K	V	I	V	S	V	Y	I	T	135
361	TAC	CCA	GCC	CGC	ACC	CGG	AAA	GTC	ATT	GTA	AGT	GTT	TAC	ATC	ACC	405
136	C	F	L	T	S	I	P	Y	Y	W	W	P	N	I	W	150
406	TGC	TTC	CTG	ACC	AGC	ATC	CCC	TAT	TAC	TGG	TGG	CCC	AAC	ATC	TGG	450
151	T	E	D	Y	I	S	T	S	V	H	H	V	L	I	W	165
451	ACT	GAA	GAC	TAC	ATC	AGC	ACC	TCT	GTG	CAT	CAC	GTC	CTC	ATC	TGG	495
166	I	H	C	F	T	V	Y	L	V	P	C	S	I	F	F	180
496	ATC	CAC	TGC	TTC	ACC	GTC	TAC	CTG	GTG	CCC	TGC	TCC	ATC	TTC	TTC	540
181	I	L	N	S	I	I	V	Y	K	L	R	R	K	S	N	195
541	ATC	TTG	AAC	TCA	ATC	ATT	GTG	TAC	AAG	CTC	AGG	AGG	AAG	AGC	AAT	585
196	F	R	L	R	G	Y	S	T	G	K	T	T	A	I	L	210
586	TTT	CGT	CTC	CGT	GGC	TAC	TCC	ACG	GGG	AAG	ACC	ACC	GCC	ATC	TTG	630
211	F	T	I	T	S	I	F	A	T	L	W	A	P	R	I	225
631	TTC	ACC	ATT	ACC	TCC	ATC	TTT	GCC	ACA	CTT	TGG	GCC	CCC	CGC	ATC	675
226	I	M	I	L	Y	H	L	Y	G	A	P	I	Q	N	R	240
676	ATC	ATG	ATT	CTT	TAC	CAC	CTC	TAT	GGG	GCG	CCC	ATC	CAG	AAC	CGC	720
241	W	L	V	H	I	M	S	D	I	A	N	M	L	A	L	255
721	TGG	CTG	GTA	CAC	ATC	ATG	TCC	GAC	ATT	GCC	AAC	ATG	CTA	GCC	CTT	765

271	R	F	R	T	M	A	A	A	T	L	K	A	F	F	K	285
811	CGG	TTC	CGC	ACC	ATG	GCA	GCC	GCC	ACG	CTC	AAG	GCT	TTC	TTC	AAG	855
286	C	Q	K	Q	P	V	Q	F	Y	T	N	H	N	F	S	300
856	TGC	CAG	AAG	CAA	CCT	GTA	CAG	TTC	TAC	ACC	AAT	CAT	AAC	TTT	TCC	900
301	I	T	S	S	P	W	I	S	P	A	N	S	H	C	I	315
901	ATA	ACA	AGT	AGC	CCC	TGG	ATC	TCG	CCG	GCA	AAC	TCA	CAC	TGC	ATC	945
316	K	M	L	V	Y	Q	Y	D	K	N	G	K	P	I	K	330
946	AAG	ATG	CTG	GTG	TAC	CAG	TAT	GAC	AAA	AAT	GGA	AAA	CCT	ATA	AAA	990
331	V	S	P	*												333
991	GTA	TCC	CCG	TGA												1002

Partial amino acid sequence of human GPCR α 19 (333 amino acids) (SEQ ID NO:20).
The seven predicted transmembrane domaines are underlined.

GPHRSQRSHLCFRAKPVFLLSTANILTVILLSQLVARRQSSYNYLLAAADILVLFFIVFVDFLLEDFILNMQMPQVP
DKIIEVLEFSSIHTSIWITVPLTIDRYIAVCHPLKYHTVSYPARTRKVIVSVYITCFLTSIPYYWPNIWTEDYISTSVH
HVLIWIHCFTVYLVPCSIFFILNSIIVYKLRRKSNFRLRGYSTGKTTAILFTISIFATLWAPRIIMILYHLYGAPIQNR
WLVHIMSDIANMLALLNTAINFFLYCFISKRFRTMAATLKAFFKCQKQPVQFYTNHNFSITSSPWISPANSHCIKMLVY
QYDKNGKPIKVSP

At the amino acid sequence level, the human GPCR α 19 is 25% identical to the *C. Elegans* F21C10.9 G-protein coupled receptor.

Nucleotide and deduced amino acid sequence of human GPCR α 20 (SEQ ID NO: 21 and 22 respectively). This nucleotide sequence is located on the chromosome 5.

1	M	L	A	A	A	F	A	D	S	N	S	S	S	M	N	15
1	ATG	CTG	GCA	GCT	GCC	TTT	GCA	GAC	TCT	AAC	TCC	AGC	AGC	ATG	AAT	45
16	V	S	F	A	H	L	H	F	A	G	G	Y	L	P	S	30
46	GTG	TCC	TTT	GCT	CAC	CTC	CAC	TTT	GCC	GGA	GGG	TAC	CTG	CCC	TCT	90
31	D	S	Q	D	W	R	T	I	I	P	A	L	L	V	A	45
91	GAT	TCC	CAG	GAC	TGG	AGA	ACC	ATC	ATC	CCG	GCT	CTC	TTG	GTG	GCT	135
46	V	C	L	V	G	F	V	G	N	L	C	V	I	G	I	60
136	GTC	TGC	CTG	GTG	GGC	TTC	GTG	GGA	AAC	CTG	TGT	GTG	ATT	GGC	ATC	180
61	L	L	H	N	A	W	K	G	K	P	S	M	I	H	S	75
181	CTC	CTT	CAC	AAT	GCT	TGG	AAA	GGA	AAG	CCA	TCC	ATG	ATC	CAC	TCC	225
76	L	I	L	N	L	S	L	A	D	L	S	L	L	L	F	90
226	CTG	ATT	CTG	AAT	CTC	AGC	CTG	GCT	GAT	CTC	TCC	CTC	CTG	CTG	TTT	270
91	S	A	P	I	R	A	T	A	Y	S	K	S	V	W	D	105
271	TCT	GCA	CCT	ATC	CGA	GCT	ACG	GCG	TAC	TCC	AAA	AGT	GTT	TGG	GAT	315
106	L	G	W	F	V	C	K	S	S	D	W	F	I	H	T	120
316	CTA	GGC	TGG	TTT	GTC	TGC	AAG	TCC	TCT	GAC	TGG	TTT	ATC	CAC	ACA	360
121	C	M	A	A	K	S	L	T	I	V	V	V	A	K	V	135
361	TGC	ATG	GCA	GCC	AAG	AGC	CTG	ACA	ATC	GTT	GTG	GTG	GCC	AAA	GTA	405
136	C	F	M	Y	A	S	D	P	A	K	Q	V	S	I	H	150
406	TGC	TTC	ATG	TAT	GCA	AGT	GAC	CCA	GCC	AAG	CAA	GTG	AGT	ATC	CAC	450
151	N	Y	T	I	W	S	V	L	V	A	I	W	T	V	A	165
451	AAC	TAC	ACC	ATC	TGG	TCA	GTG	CTG	GTG	GCC	ATC	TGG	ACT	GTG	GCT	495
166	S	L	L	P	L	P	E	W	F	F	S	T	I	R	H	180
496	AGC	CTG	TTA	CCC	CTG	CCG	GAA	TGG	TTC	TTT	AGC	ACC	ATC	AGG	CAT	540
181	H	E	G	V	E	M	C	L	V	D	V	P	A	V	A	195
541	CAT	GAA	GGT	GTG	GAA	ATG	TGC	CTC	GTG	GAT	GTA	CCA	GCT	GTG	GCT	585
196	E	E	F	M	S	M	F	G	K	L	Y	P	L	L	A	210
586	GAA	GAG	TTT	ATG	TCG	ATG	TTT	GGT	AAG	CTC	TAC	CCA	CTC	CTG	GCA	630
211	F	G	L	P	L	F	F	A	S	F	Y	F	W	R	A	225
631	TTT	GGC	CTT	CCA	TTA	TTT	TTT	GCC	AGC	TTT	TAT	TTC	TGG	AGA	GCT	675
226	Y	D	Q	C	K	K	R	G	T	K	T	Q	N	L	R	240
676	TAT	GAC	CAA	TGT	AAA	AAA	CGA	GGA	ACT	AAG	ACT	CAA	AAT	CTT	AGA	720
241	N	Q	I	R	S	K	Q	V	T	V	M	L	L	S	I	255
721	AAC	CAG	ATA	CGC	TCA	AAG	CAA	GTC	ACA	GTG	ATG	CTG	CTG	AGC	ATT	765
256	A	I	I	S	A	L	L	W	L	P	F	W	V	A	W	270

271	L	W	V	W	H	L	K	A	A	G	P	A	P	P	Q	285
811	CTG	TGG	GTA	TGG	CAT	CTG	AAG	GCT	GCA	GGC	CCG	GCC	CCA	CCA	CAA	855
286	G	F	I	A	L	S	Q	V	L	M	F	S	I	S	S	300
856	GGT	TTC	ATA	GCC	CTG	TCT	CAA	GTC	TTG	ATG	TTT	TCC	ATC	TCT	TCA	900
301	A	N	P	L	I	F	L	V	M	S	E	E	F	R	E	315
901	GCA	AAT	CCT	CTC	ATT	TTT	CTT	GTG	ATG	TCG	GAA	GAG	TTC	AGG	GAA	945
316	G	L	K	G	V	W	K	W	M	I	T	K	K	P	P	330
946	GGC	TTG	AAA	GGT	GTA	TGG	AAA	TGG	ATG	ATA	ACC	AAA	AAA	CCT	CCA	990
331	T	V	S	E	S	Q	E	T	P	A	G	N	S	E	G	345
991	ACT	GTC	TCA	GAG	TCT	CAG	GAA	ACA	CCA	GCT	GGC	AAC	TCA	GAG	GGT	1035
346	L	P	D	K	V	P	S	P	E	S	P	A	S	I	P	360
1036	CTT	CCT	GAC	AAG	GTT	CCA	TCT	CCA	GAA	TCC	CCA	GCA	TCC	ATA	CCA	1080
361	E	K	E	K	P	S	S	P	S	S	G	K	G	K	T	375
1081	GAA	AAA	GAG	AAA	CCC	AGC	TCT	CCC	TCC	TCT	GGC	AAA	GGG	AAA	ACT	1125
376	E	K	A	E	I	P	I	L	P	D	V	E	Q	F	W	390
1126	GAG	AAG	GCA	GAG	ATT	CCC	ATC	CTT	CCT	GAC	GTA	GAG	CAG	TTT	TGG	1170
391	H	E	R	D	T	V	P	S	V	Q	D	N	D	P	I	405
1171	CAT	GAG	AGG	GAC	ACA	GTC	CCT	TCT	GTA	CAG	GAC	AAT	GAC	CCT	ATC	1215
406	P	W	E	H	E	D	Q	E	T	G	E	G	V	K	*	419
1216	CCC	TGG	GAA	CAT	GAA	GAT	CAA	GAG	ACA	GGG	GAA	GGT	GTT	AAA	TAG	1260

Amino acid sequence of human GPCR \times 20 (419 amino acids) (SEQ ID NO:22). The seven predicted transmembrane domaines are underlined.

MLAAAFADSNSSSMNVSF~~FAHLHFAGGYLP~~SDSQDWRTIIPALLVAVCLVGVGNLCVIGILLHNAWKGPMSIHSLILNL
SLADLSLLLFSAPIRATAYSKSVWDLGWVCKSSDWFIHTCMAAKSLTIVVVAKVCFMYASDPAKQVSIHNYTIWSVLVA
IWTVASLLPLPEWFFSTIRHHEGVEMCLVDVPAVAEEFMSMFGKLYPLLAFLPLFFASFYFWRAYDQCKKRGTKTQNLN
NQIRSKQVTVMLLSIAIISALLWLP~~EWVAVLWVWHLKAAGPAPPQGFIALSQVLMFS~~ISSANPLIFLVMSEEFREGKGV
WKWMITKKPPTVSESQETPAGNSEGLPKVPSPESPASIP~~EKEKPSSSGKGKTEKAEIPILPDVEQFWHERD~~TVPSVQ
DNDPIPWEHEDQETGEGVK

At the amino acid sequence level, the human GPCR \times 20 is 20% identical to the mouse galanin 2 receptor.

CLAIMS

1. A G-protein coupled receptor having an amino acid sequence which presents more than 75% sequence identity with the sequence SEQ ID NO. 1.
- 5 2. The G-protein coupled receptor according to claim 1, having an amino acid sequence which presents more than 80% sequence identity with the sequence SEQ ID NO. 1.
3. The G-protein coupled receptor according
10 to claim 1, having an amino acid sequence which presents more than 85% sequence identity with the sequence SEQ ID NO. 1.
4. The G-protein coupled receptor according to claim 1, having an amino acid sequence which presents
15 more than 90% sequence identity with the sequence SEQ ID NO. 1.
5. The G-protein coupled receptor according to claim 1, having an amino acid sequence which presents more than 95% sequence identity with the sequence
20 SEQ ID NO. 1.
6. The G-protein coupled receptor having the amino acid sequence SEQ ID NO. 1 or a specific active portion thereof.
7. A polynucleotide encoding any of the
25 amino acid sequences of the G-protein coupled receptor according to any of the preceding claims 1 to 6.
8. An agonist, reverse agonist, antagonist or inhibitor of the receptor or the polynucleotide according to any of the preceding claims 1 to 7.
- 30 9. A vector comprising the polynucleotide

according to the claim 9.

11. A non-human mammal comprising a partial or total deletion of the polynucleotide according to the claim 8 encoding the receptor according to any of the preceding claims 1 to 6, preferably an non-human mammal
5 comprising an homologous recombination "knock-out" of said polynucleotide or a transgenic non-human mammal overexpressing above natural level said polynucleotide.

12. A method for the screening (detection and possibly recovering) of compounds or natural extract which
10 are known or not known to be agonists, antagonists or inhibitors to the receptor according to any of the preceding claims 1 to 6, said method comprising :

- contacting a cell or cell extract from the cell transfected with a vector according to the claim 9,
- 15 - possibly isolating a membrane fraction from the cell extract or the complete cell with a compound binding to said receptor under conditions permitting binding of said compound or molecules present in said natural extract to said receptor, possibly by the activation of
20 a functional response, and
- detecting the presence of any such compound or molecules by means of a bioassay (preferably a modification in the production of a second messenger or an increase in the receptor activity) in the presence of the other known
25 compound working as an agonist, reverse agonist, antagonist or inhibitor to the receptor and thereby recovering and determining whether said unknown compound or molecule(s) is (are) able to work as an agonist, antagonist or inhibitor of the compound to its receptor.

30 13. An unknown compound or molecule(s), identified by the screening method according to the claim

14. A pharmaceutical composition comprising an adequate pharmaceutical carrier and a sufficient amount

of the compound or molecules according to the claim 8 or 13.

15. Use of the pharmaceutical composition according to the claim 14, for the manufacture of a
5 medicament in the prevention and/or the treatment of a disease selected from the group consisting of viral infections or diseases induced by various viruses or bacteria, the treatment of disturbances of cell migration, diseases or perturbations of the immune system, including
10 cancer, development of tumours and tumour metastasis, inflammatory and neo-plastic processes, bacterial and fungal infections, for wound and bone healing and dysfunction of regulatory growth functions, pains, diabetes, obesity, anorexia, bulimia, acute heart failure,
15 hypotension, hypertension, urinary retention, osteoporosis, angina pectoris, myocardial infarction, restenosis, atherosclerosis, diseases characterised by excessive smooth muscle cell proliferation, aneurysms, wound healing, diseases characterised by loss of smooth muscle cells or
20 reduced smooth muscle cell proliferation, stroke, ischemia, ulcers, allergies, benign prostatic hypertrophy, migraine, vomiting, psychotic and neurological disorders, including anxiety, schizophrenia, maniac depression, depression, delirium, dementia and severe mental retardation,
25 degenerative diseases, neurodegenerative diseases such as Alzheimer's disease or Parkinson's disease, and dyskinasias, such as Huntington's disease or Gilles de la Tourett's syndrome and other related diseases.

16. Use of the pharmaceutical composition
30 according to the claim 14, for the manufacture of a medicament in the prevention and/or the treatment of blood

17. Diagnostic kit comprising all the media and means for detecting the receptor and nucleotide sequence encoding it or an activity of said receptor and nucleotide sequence encoding it according to any of the 5 preceding claims 1 to 8.

1/1

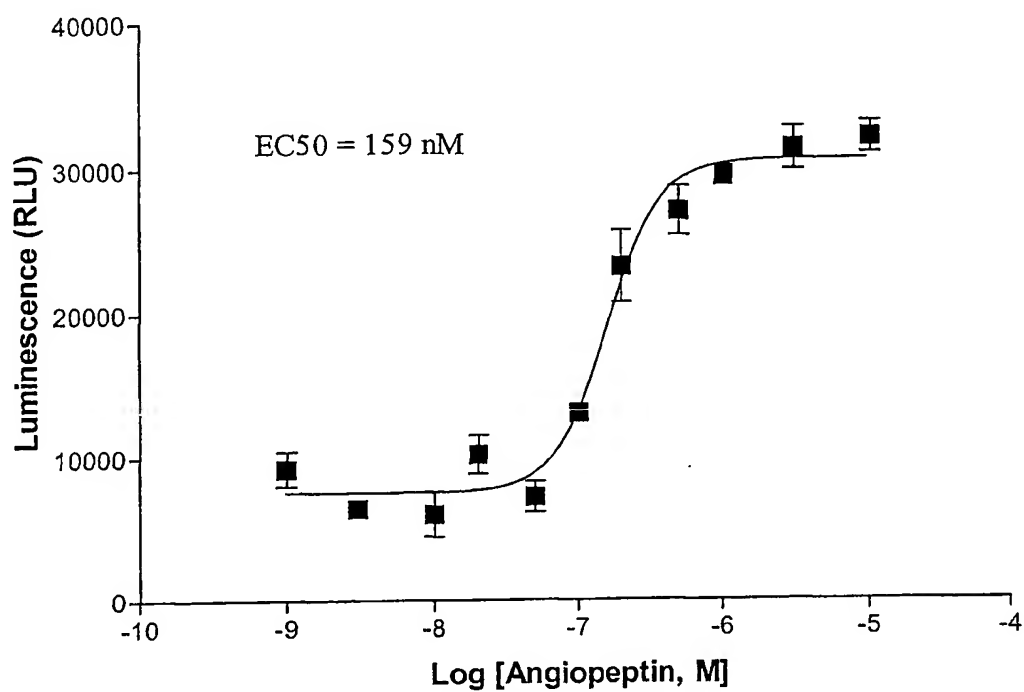


Figure 1 : Dose response curve with angiopeptin

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- Published:**
- with international search report
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(54) Title: A RECOMBINANT CELL LINE EXPRESSING GPCR α 11 AS A FUNCTIONAL RECEPTOR VALIDATED BY ANGIOPEPTIN AND USEFUL FOR SCREENING OF AGONISTS AND ANTAGONISTS

ABSTRACT

reference reagents. GPCR α 11 cells give a specific signal with synthetic angiopeptin and a somatostatin analog, allowing to validate this cell line for screening of natural or synthetic agonists and antagonists. In parallel, extended tissue distribution and polyclonal antibodies have been produced to facilitate GPCR α 11 characterisation.

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/BE 01/00104

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07K14/72

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, EMBL

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	WO 01 16159 A (SMITHKLINE BEECHAM CORP) 8 March 2001 (2001-03-08) SEQ ID NO: 2; Claim 1	1-7, 9-12
P, X	WO 01 36471 A (ARENA PHARMACEUTICALS INC ; CHEN RUOPING (US); DANG HUONG T (US); L) 25 May 2001 (2001-05-25) SEQ ID NO: 30, Claim 57	1-7, 9-12
P, X	WO 01 19983 A (DELEERSNIJDER WILLY ; HEUVAERT NICOLE D (BE); NYS GUY (BE); SOLVAY) 22 March 2001 (2001-03-22) SEQ ID NO: 2, claims	1-7, 9-12
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☒ Further documents are listed in the continuation of box C

☒ Patent family members are listed in annex.

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G document member of the same patent family

Date of the actual completion of the international search

Date of mailing of the international search report

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Name of the ISA

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/BE 01/00104

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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E	WO 01 48189 A (MATSUMOTO SHUN ICHIRO ; MORIKAWA NORIYUKI (JP); SUGIYAMA TOMOYASU () 5 July 2001 (2001-07-05) SEQ ID NO: 44 ----	1-7,9,10
A	WO 99 32519 A (FORTIN YVES ; LEMBO PAOLA (CA); AHMAD SULTAN (CA); BANVILLE DENIS () 1 July 1999 (1999-07-01) -----	

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 8, 13-17

Claims 8 and 13 refer to an agonist/antagonist of the polypeptide respectively to an unknown compound identified by the method of Claim 12 without giving a true technical characterization. Moreover, no such compounds are defined in the application. In consequence, the scope of said claims is ambiguous and vague, and their subject-matter is not sufficiently disclosed and supported (Art. 83 and 84 EPC). No search can be carried out for purely speculative claims whose wording is, in fact, a mere recitation of the results to be achieved. Consequently neither for Claims 14 to 16 which relate to the use of said compounds a search could be carried out.

The same, in principle applies for the "kit" of Claim 17 wherein none of the "media and means" which are essential for said kit are identified.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/BE 01/00104

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